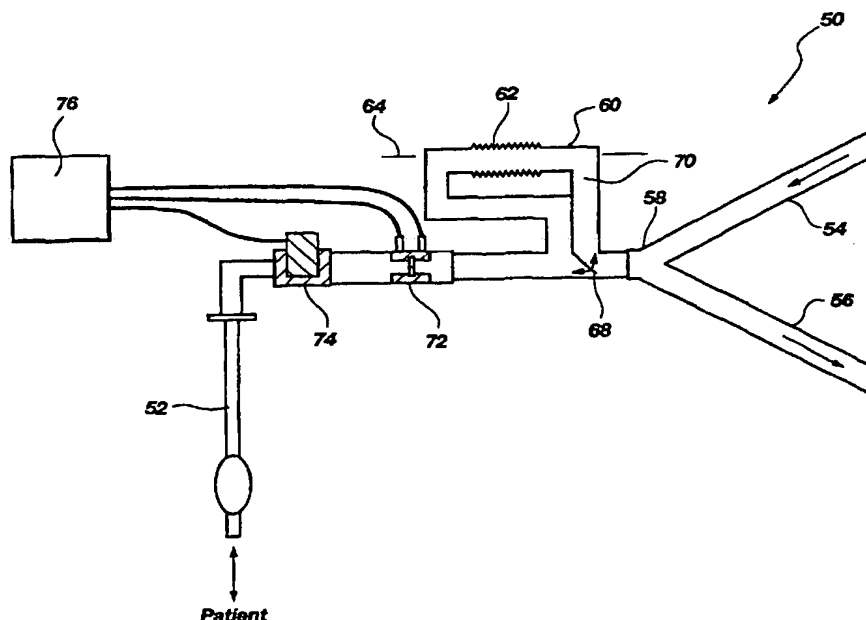




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(54) Title: APPARATUS AND METHOD FOR NON-INVASIVELY MEASURING CARDIAC OUTPUT



(57) Abstract

Apparatus and methods for non-invasively determining cardiac output using partial re-breathing techniques are disclosed in which the apparatus is constructed with an instantaneously adjustable deadspace (70) for accommodating differences in breathing capacities various patients. The apparatus (50) is constructed of inexpensive elements, including a single two-way valve (22) which renders the apparatus very simple to use and inexpensive so that the unit may be readily disposable. The method of the invention provides a novel means (46) of estimating cardiac output based on alveolar CO₂ values rather than end-tidal CO₂ values as previously practiced. A program for calculating cardiac output is also disclosed.

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APPARATUS AND METHOD FOR NON-INVASIVELY MEASURING CARDIAC OUTPUT

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BACKGROUND

Field of the Invention: This invention relates to non-invasive means of determining cardiac output in patients, and specifically relates to partial re-breathing systems and methods for determining cardiac output in patients.

Statement of the Art: It is important in many medical procedures to
10 determine or monitor the cardiac output of a patient. Techniques are known and used in the art which employ the use of catheters inserted at certain arterial points (e.g., femoral artery, jugular vein, etc.) to monitor blood temperature and pressure in order to determine cardiac output of the patient. Although such techniques can produce a reasonably accurate result, the invasive nature of the procedure has high
15 potential for morbidity and mortality consequences.

Adolph Fick's measurement of cardiac output, first proposed in 1870, has served as the standard by which all other means of determining cardiac output have been evaluated since that date. Fick's well-known equation, written for CO₂, is:

$$Q = \frac{V_{CO_2}}{(C_{vCO_2} - C_{aCO_2})}$$

20 where Q is cardiac output, V_{CO₂} is the amount of CO₂ excreted by the lungs and C_{aCO₂} and C_{vCO₂} are the arterial and venous CO₂ concentrations, respectively.

Notably, the Fick Equation presumes an invasive method (i.e., catheterization) of calculating cardiac output because the arterial and mixed venous blood must be sampled in order to determine arterial and venous CO₂ concentrations.

25 It has previously been shown, however, that non-invasive means may be used for determining cardiac output while still using principles embodied in the Fick Equation. That is, expired CO₂ ("pCO₂") levels can be monitored to estimate arterial CO₂ concentrations and a varied form of the Fick Equation can be applied to evaluate observed changes in pCO₂ to estimate cardiac output. One use of the Fick
30 Equation to determine cardiac output in non-invasive procedures requires the

comparison of a "standard" ventilation event to a sudden change in ventilation which causes a change in expired CO_2 values and a change in excreted volume of CO_2 . The commonly practiced means of providing a sudden change in effective ventilation is to cause the ventilated patient to re-breathe a specified amount of
5 previously exhaled air. This technique has commonly been called "re-breathing."

Prior methods of re-breathing have used the partial pressure of end-tidal CO_2 to approximate arterial CO_2 while the lungs act as a tonometer to measure venous CO_2 . That method of re-breathing has not proven to be a satisfactory means of measuring cardiac output because the patient is required to breath directly into and
10 from a closed volume in order to produce the necessary effect. However, it is usually impossible for sedated or unconscious patients to actively participate in inhaling and exhaling into a bag. The work of some researchers demonstrated that the Fick Equation could be further modified to eliminate the need to directly calculate venous P_{CO_2} (P_{vCO_2}) by assuming that the P_{vCO_2} does not change within the
15 time period of the perturbation- an assumption that could be made by employing the partial re-breathing method. (See, Capek et al., "Noninvasive Measurement of Cardiac Output Using Partial CO_2 Rebreathing", IEEE Transactions On Biomedical Engineering, Vol. 35, No. 9, September 1988, pp. 653-661.)

Known partial re-breathing methods are advantageous over invasive
20 measuring techniques because they 1) are non-invasive, 2) use the accepted Fick principle of calculation, 3) are easily automated, 4) require no patient cooperation and 5) allow cardiac output to be calculated from commonly monitored clinical signals. However, known partial re-breathing methods have significant disadvantages as well. Specifically, known methods 1) are less accurate with non-
25 intubated or spontaneously breathing patients, 2) only allow intermittent measurements (usually about every four minutes), 3) result in an observed slight, but generally clinically insignificant, increase in arterial CO_2 levels, and 4) do not permit measurement of shunted blood flow (that is, blood which does not participate in gas exchange). Further, known apparatus used for partial re-breathing techniques
30 are of standard construction and do not compensate for differences in patient size or capacities. In addition, many devices employ expensive elements, such as three-way valves which render the devices too expensive to be used as disposable units.

Thus, it would be advantageous to provide a means of measuring cardiac output using partial re-breathing techniques which 1) overcome the disadvantages of prior systems, 2) provide better and more continuous measurement, and 3) require less expensive equipment thereby making the device suitable for manufacturing as a single-use, or disposable, product. It would also be advantageous to provide partial re-breathing apparatus which is instantaneously adjustable to compensate for various sizes and capacities of patients. Further, it would be advantageous to provide new methods of estimating cardiac output based on alveolar CO₂ output rather than end tidal CO₂ as is currently used in the art.

SUMMARY OF THE INVENTION

In accordance with the present invention, apparatus and methods for measuring cardiac output using a modified Fick Equation are provided where the amount of deadspace which is provided in the apparatus can be adjusted to increase or decrease the volume of exhalate to be re-breathed by the patient, thereby decreasing ventilation without changing airway pressure. The apparatus and methods of the present invention also provide an adjustability factor which enables the apparatus to be adjusted to suit any size or capacity of patient. The apparatus of the present invention also employs significantly less expensive elements of construction thereby rendering the device disposable.

The apparatus and methods of the present invention apply a modified Fick Equation to calculate changes in pCO₂ flow and concentration to evaluate cardiac output. The traditional Fick Equation, written for CO₂ is:

$$Q = \frac{V_{CO_2}}{(C_{vCO_2} - C_{aCO_2})}$$

where Q is cardiac output (when calculated using re-breathing techniques referred to as pulmonary capillary blood flow or "PCBF"), V_{CO₂} is the output of CO₂ from the lungs and C_{aCO₂} and C_{vCO₂} are the arterial and venous CO₂ concentrations, respectively. It has been shown in prior work of others that cardiac output can be

estimated from calculating the change in $p\text{CO}_2$, as estimated by end-tidal CO_2 ("et CO_2 "), as a result of a sudden change in ventilation. That can be done by applying a differential form of the Fick Equation as follows:

$$Q = \frac{V_{\text{CO}_2_1}}{(C_{v_1} - C_{a_1})} = \frac{V_{\text{CO}_2_2}}{(C_{v_2} - C_{a_2})}$$

- 5 where C_a is arterial CO_2 concentration, C_v is venous CO_2 concentration, and the subscripts 1 and 2 reference measured values before a change in ventilation and measured values during a change in ventilation, respectively. The differential form of the Fick Equation can, therefore, be rewritten as:

$$Q = \frac{V_{\text{CO}_2_1} - V_{\text{CO}_2_2}}{(C_{v_1} - C_{a_1}) - (C_{v_2} - C_{a_2})}$$

or

$$Q = \frac{\Delta V_{\text{CO}_2}}{\Delta C_{a_{\text{CO}_2}}} = \frac{\Delta V_{\text{CO}_2}}{s \Delta \text{etCO}_2}$$

- 10 where ΔV_{CO_2} is the change in CO_2 production in response to the change in ventilation, $\Delta C_{a_{\text{CO}_2}}$ is the change in arterial CO_2 concentration in response to the change in ventilation, ΔetCO_2 is the change in end-tidal CO_2 concentration and s is the slope of the CO_2 dissociation curve. The foregoing differential equation assumes that there is no appreciable change in venous CO_2 concentration during the
- 15 re-breathing episode, as demonstrated by Capek, et al., in their previous work. Also, a dissociation curve, well-known in the art, is used for determining CO_2 concentration based on partial pressure measurements.

- In previous partial re-breathing methods, a deadspace, usually comprising an additional 50-250 ml capacity of air passage, was provided in the ventilation circuit
- 20 to decrease the effective alveolar ventilation. In the present invention, a ventilation apparatus is provided with an adjustable deadspace to provide the necessary change in ventilation for determining accurate changes in CO_2 production and end-tidal CO_2

commensurate with the requirements of differently sized patients. In one embodiment of the ventilation apparatus, selectively adjustable deadspace is provided through which the patient exhales and inhales. Thus, the adjustable deadspace of the apparatus permits easy adjustment of the deadspace to
5 accommodate any size or capacity of patient, from a small to a large adult. As a result, the patient is provided with a volume of re-breathable gas commensurate with the patient's size which decreases effective ventilation without changing the airway pressure. Because airway and intra-thoracic pressure are not affected by the re-breathing method of the present invention, cardiac output is not significantly
10 affected by re-breathing. In an alternative method, the deadspace may be effectively lessened by selectively leaking exhaled gas from the ventilation system to atmosphere or to a closed receptacle means during inspiration.

The ventilation apparatus of the present invention includes a tubular portion which is placed in contact with the patient, and an inhalation conduit and exhalation
15 conduit. In a common configuration, the inhalation conduit and exhalation conduit may be interconnected between a ventilator unit and the patient. Alternatively, however, a ventilator unit (i.e., a source of deliverable gas mechanically operated to assist the patient in breathing) need not be used with the ventilation apparatus and inhaled and exhaled breath is merely taken from or vented to atmosphere. Other
20 conventional equipment commonly used with ventilator units or used in ventilation of a patient may be used with the inventive ventilation apparatus, such as a breathing mask.

An electrical pneumotachometer for measuring flow of gas and a capnograph for measuring CO₂ concentrations are provided in proximity to the tubular portion
25 between the inhalation and exhalation portions of the ventilation apparatus and the patient's lungs. The pneumotachometer and capnograph serve as detection apparatus for detecting changes in gas concentrations and flow and are in electrical communication with a computer having software designed to store and evaluate the measurements taken by the detection apparatus in real time. Other forms of
30 detection apparatus may be used. Adjustable deadspace means are provided in connection with the exhalation portion of the ventilation apparatus, and may interconnect with the inhalation portion of the ventilation apparatus. In one embodiment, the adjustable deadspace means may be manually adjusted.

Alternatively, electromechanical means may be interconnected between the computer and the adjustable deadspace means to provide automatic adjustment of the deadspace volume responsive to the size or capacity of the patient and responsive to changes in ventilation.

5 In an alternative embodiment, a tracheal gas insufflation apparatus is used to provide the change in ventilation necessary to calculate pulmonary CO_2 changes using the differential Fick Equation. Tracheal gas insufflation ("TGI") apparatus is commonly used to flush the deadspace of the alveolar spaces of the lungs and to replace the deadspace with fresh gas infused through insufflation means. That is,
10 fresh gas is introduced to the central airway to improve alveolar ventilation and/or to minimize ventilatory pressure requirements. TGI apparatus is interconnected to a ventilator system and includes a means of introducing fresh gas into the breathing tube as it enters the patient's lungs. The TGI apparatus may be used in the methods of the present invention to determine baseline measurements of VCO_2 and etCO_2 .
15 during TGI. When the TGI system is turned off, a deadspace is formed by the patient's trachea and the endo-tracheal tube of the TGI apparatus which allows measurement of a change in CO_2 to be evaluated in accordance with the invention. Further, the catheter of the TGI apparatus may be variably positioned within the trachea of the patient to further adjust the deadspace volume.

20 The deadspace provided in the apparatus of the present invention causes a rapid drop in VCO_2 which thereafter increases slightly and slowly as the functional residual lung gas capacity equilibrates with the increase in alveolar CO_2 level. The change in etCO_2 rises more slowly after the addition of deadspace, depending on alveolar deadspace and cardiac output, but then stabilizes to a new level. A
25 "standard," or baseline, breathing episode is conducted for a selected period of time immediately preceding the introduction of a deadspace (i.e., rebreathing) and VCO_2 and etCO_2 values are determined based on measurements made during the "standard" breathing event. Those values are substituted as the values VCO_{2_1} and $\text{C}_{\text{aCO}_{2_1}}$ in the differential Fick Equation. VCO_2 and etCO_2 values are also
30 determined from measurements taken approximately thirty seconds following the introduction of a deadspace during partial rebreathing to provide the second values (subscript 2 values) in the differential Fick Equation. The period of time during

which partial rebreathing occurs and during which normal breathing occurs may be determined by the individual size and lung capacity of the patient. Additionally, the period of time between a rebreathing episode and a subsequent normal breathing episode may vary between patients depending on a particular patient's size and
5 breath capacity. Thus, a thirty second time period for a breathing episode is only an average time and may be greater or lesser.

Cardiac output is determined, in the present invention, by estimating alveolar CO_2 concentration rather than basing output on end-tidal CO_2 concentration, as is practiced in the prior art. Partial pressure values that are obtained from CO_2
10 measurements are converted to a value for gas content in the blood using the dissociation equation known in the art. Thus, a more accurate cardiac output can be determined. In addition, the accuracy of cardiac output is increased by correcting VCO_2 values to account for flow of CO_2 into the functional residual capacity of the lungs, defined as the volume of gas left in the lungs at the end of an expired breath.
15 The determination of values based on experiential data are processed by the software program to determine cardiac output.

The ventilation apparatus of the present invention employs inexpensive yet accurate monitoring systems as compared to the systems currently used in the art. The methods of the invention allow automatic adjustability of the apparatus for
20 accommodating patients of different sizes and provides consistent monitoring with modest recovery time. Further, the present apparatus and methods can be used equally with non-responsive, intubated patients as well as non-intubated, responsive patients.

25 BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, which illustrate what is currently considered to be the best mode for carrying out the invention:

FIG. 1 is a schematic representation of conventional ventilation systems used for assisting patient breathing;

30 FIG. 2 is a schematic representation of prior art re-breathing systems;

FIG. 3 is a schematic first embodiment of the ventilation apparatus of the present invention illustrating an adjustably expandable deadspace;

FIG. 4 is a schematic representation of an alternative embodiment of the present invention where the re-breathing circuit is constructed with a leak valve;

FIGS. 5(a)-(c) are a schematic representation of another alternative embodiment of the present invention where the inhalation portion and exhalation portion of the ventilation circuit are interconnected and have a two-way closeable valve;

FIG. 6 is a schematic representation of an alternative embodiment similar to the embodiment shown in FIG. 5, but where the inhalation and exhalation portions are adjustably expandable;

FIG. 7 is a schematic representation of another embodiment of the invention where a series of valves are provided along the length of the inhalation and exhalation portions to provide a selectable volume of deadspace dependent upon the size and/or capacity of the patient;

FIGS. 8(a) and (b) are schematic representations of another embodiment of the invention where a leak valve is provided, both with a vent to atmosphere and to a parallel compliance chamber;

FIG. 9 is a schematic representation of a tracheal gas insufflation apparatus of the present invention which can be used to provide a necessary change in ventilation with a deadspace;

FIG. 10 is a schematic representation of human lungs illustrating the concepts of parallel deadspace, alveolar deadspace and serial deadspace in the lungs of a patient; and

FIG. 11 is a flow diagram briefly describing the calculations made in the software program to calculate cardiac output from the measured values of normal breathing and partial rebreathing.

DETAILED DESCRIPTION OF THE ILLUSTRATIONS

For comparative purposes, FIG. 1 schematically illustrates a conventional ventilation system which is typically used with patients who require assisted breathing during an illness, a surgical procedure or recovery from a surgical procedure. The conventional ventilator system 10 includes a tubular portion 12 which is inserted into the trachea by intubation procedures. The distal end 14 of the tubular portion 12 is fitted with a Y-piece 16 which interconnects an inspiratory

hose 18 and an expiratory hose 20. Both the inspiratory hose 18 and expiratory hose 20 are connected to a ventilator machine (not shown) which delivers air to the inspiratory hose 18. A one-way valve 22 is positioned on the inspiratory hose to prevent exhaled gas from entering the inspiratory hose 18 beyond the valve 22. A similar one-way valve 24 on the expiratory hose 20 limits movement of inspiratory gas into the expiratory hose 20. Exhaled air flows passively into the expiratory hose 20.

In known re-breathing ventilation circuits 30, as shown in FIG. 2, the tubular portion 32 is inserted into the trachea of the patient by intubation procedures, and gas is provided to the patient from a ventilator machine (not shown) via an inspiratory hose 34 which is interconnected by a Y-piece 36 to an expiratory hose 38. An additional length of hose 40 is provided between the tubular portion 32 and the Y-piece 36 which acts as a deadspace for receiving exhaled gas. A three-way valve 42 generally positioned between the Y-piece 36 and the opening to the additional length of hose 40 is constructed for intermittent actuation to selectively direct the flow of gas. That is, at one setting, the valve 42 allows inspiratory gas to enter the tubular portion 32 while preventing movement of the gas into the additional length of hose 40. In a second setting, the valve 42 allows exhaled gas to enter into the expiratory hose 38 while preventing movement of gas into the additional length of hose 40. In a third setting, the three-way valve 42 directs exhaled air to enter into the additional length of hose 40 and causes the patient to re-breathe the exhaled air on the following breath to thereby cause a change in effective ventilation.

The change in VCO_2 and end-tidal CO_2 caused by the change in ventilation in the prior art system of FIG. 2 can then be used to calculate cardiac output. Sensing and/or monitoring devices may be attached to the re-breathing ventilation circuit 30 between the additional length of hose 40 and the tubular portion 32. The sensing and/or monitoring devices may include, for example, means 44 for detecting CO_2 concentration and means 46 for detecting flow parameters during inhalation and exhalation. Those sensing and/or monitoring devices are typically connected to data recording and display equipment (not shown). One problem encountered in use of the prior art system is that the deadspace provided by the additional length of hose 40 is fixed and may not be adjusted. As a result, the

amount of deadspace provided in the circuit for a small adult to effect re-breathing is the same amount of deadspace available for a large adult to effect re-breathing, and the resulting changes in CO₂ values for patients of different size, derived from fixed-deadspace systems, can produce inadequate evaluation of cardiac output.

- 5 Further, the three-way valve 40 of the system is expensive and significantly increases the cost of the ventilation device.

FIG. 3 illustrates the ventilation apparatus of the present invention which provides an improvement over known ventilation devices used to detect or monitor cardiac output. The present ventilation apparatus 50 comprises a tubular air-way 52
10 which is placed in communication with the patient's lungs. Although the present ventilation apparatus 50 may be placed in communication with the trachea by intubation procedures as is done in the prior art, the present ventilation apparatus 50 need not be inserted directly into the trachea of the patient. Alternatively, a breathing mask may be used for positioning over the patient's nose and mouth.
15 Thus, the present invention may be used with unconscious or uncooperative patients needing ventilation assistance and may be used with equal efficacy with patients who are conscious. The ventilation apparatus 50 also includes an inspiratory hose 54 and an expiratory hose 56 which may be each ventilated to atmosphere or may be connected to a ventilator machine (not shown) which provides gas for delivery to
20 the patient through the inspiratory hose 54. The inspiratory hose 54 and expiratory hose 56 may be joined together by a Y-piece 58.

The Y-piece 58 connects to an additional length of conduit or hose 60 which provides a deadspace for receiving exhaled gas from the patient. However, the additional length of hose 60 is structured to be selectively expandable to readily
25 enable the volume of deadspace to be adjusted commensurate with the size or lung capacity of the patient, or to other ventilation parameters, such as increased or decreased tidal volume or modified respiration rate. As suggested by the schematic drawing of FIG. 3, selective expansion of the deadspace may be accomplished by structuring the additional length of hose 60 with an expandable section 62 made of,
30 for example, a piece of corrugated hose which can be lengthened or shortened by simply pulling or pushing the expandable section 62 along its longitudinal axis 64. The corrugated hose will retain the length at which it is positioned until adjusted again. Other suitable means of providing adjustable expansion of the volume of the

deadspace are available, extending the length of the hose 60 being but one approach. A three-way valve 68 may be connected to the additional length of hose 60 to force inspiratory gas to enter the deadspace 70 upon inhalation. The three-way valve 68 is also structured to selectively prevent exhaled gas from entering the deadspace 70 during normal breathing or to direct exhaled gas into deadspace 70 during re-breathing episodes so that the patient is forced to re-breathe exhaled gas from the deadspace 70.

A flow meter 72, or pneumotachometer, is attached to the ventilation apparatus 50 at a point between the tubular air-way 52 and the additional length of hose 60. The flow meter 72 detects gas flow through the ventilation apparatus 50. A CO₂ sensor 74, or capnograph, is also connected to the ventilation apparatus 50 between the tubular air-way 52 and the additional length of hose 60. The CO₂ sensor 74 detects changes in CO₂ resulting from a change in ventilation, the data from which is used to calculate cardiac output. The CO₂ sensor 74 may be an "on airway" sensor, a sampling sensor of the type which withdraws a side stream sample of gas for testing, or any other suitable CO₂ sensor. Both the flow meter 72 and CO₂ sensor 74 are connected to a computer 76 which is programmed to store and analyze data from the flow meter 72 and CO₂ sensor 74, and to calculate from the data the estimated cardiac output of the patient.

As previously described herein, the differential Fick Equation requires a change in pulmonary gas concentration and output to be induced in the patient in order to estimate cardiac output. Re-breathing gas previously exhaled by the patient increases the amount of CO₂ breathed in by the patient and enables the evaluation of increased CO₂ levels during a change in effective ventilation as compared to standard CO₂ levels during normal ventilation. The ventilation apparatus of the present invention provides the ability to selectively adjust the deadspace required in re-breathing to increase the amount of gas (CO₂) re-breathed by the patient from the previous exhalation. The ventilation apparatus of the present invention also allows the ventilation circuit to be adjusted automatically in accordance with the size or capacity of a patient, and in response to ventilation parameters. That is, if the detected change in etCO₂ is less than 3 mm Hg, or the change in VCO₂ is less than 0.2 times the VCO₂, then the deadspace volume should be increased by twenty percent.

In an alternative embodiment of the apparatus 50 of the invention, as shown in FIG. 4, the expense of using a three-way valve may be eliminated by structuring the additional length of hose 60 with an inexpensive two-way valve 78 and by positioning a flow restrictor 80 between the inlet 82 and outlet 84 of the deadspace 70. Thus, when the two-way valve 78 is closed, gas to and from the ventilator machine will be directed through the flow restrictor 80 and to the patient. During a re-breathing episode, the two-way valve 78 is open so that the exhaled air, encountering the flow restrictor 80, follows the course of less resistance through the deadspace 70. Thus, the deadspace 70 may be adjusted at the expandable section 62 to provide the necessary deadspace 70 for calculating changes in cardiac output.

In another alternative embodiment of the ventilation apparatus 50 of the present invention, as shown in FIGS. 5(a)-(c), a shunt line 84 is positioned between the inspiratory hose 54 and the expiratory hose 56 to provide selective sized deadspace 70 in the circuit. The structure of the embodiment shown in FIGS. 5(a)-(c) causes the inspiratory hose 54 and expiratory hose 56 to act as part of the deadspace 70, as well. A two-way shunt valve 86 positioned on the shunt line 84 selectively directs the flow of inspired and expired gas dependent upon whether the shunt valve 86 is open or closed. Thus, when the ventilation apparatus 50 is configured for normal or baseline breathing, as depicted in FIG. 5(a), exhaled air (represented by the shaded area) will enter the expiratory hose 56. During normal breathing, the shunt valve 86 is closed. When the ventilation apparatus 50 is configured for a re-breathing episode, as depicted in FIG. 5(b), the shunt valve 86 is opened and exhaled gas may fill a portion of the inspiratory hose 54, all of the expiratory hose 56 and the shunt line 84, all of which serve as the deadspace 70.

The deadspace 70 in the embodiment shown in FIGS. 5(a)-(c) may be rendered adjustably expandable, as shown in FIG. 6, by structuring the inspiratory hose 54 with an expandable section 90 positioned between the shunt line 84 and the Y-piece 58, and by structuring the expiratory hose 56 with an expandable section 92 positioned between the shunt line 84 and the Y-piece 58. Thus, the deadspace 70 can be selectively adjusted in accordance with the size or capacity of the patient, or responsive to operating conditions, by increasing that portion of the inspiratory hose 54 and expiratory hose 56 extending from the Y-piece 58. Any suitable adjustably expandable means may be used. As suggested by FIG. 6, however, the expandable

section 90, 92 may be made from corrugated plastic material the length of which can be easily expanded or contracted, and the plastic material will maintain its adjusted length until repositioned. The embodiment of FIG. 6 provides a particularly simple and inexpensive construction rendering a particularly preferred
5 embodiment because of its ease of use and disposability.

In yet another embodiment of the ventilation apparatus 50 of the present invention, as shown in FIG. 7, the amount of available deadspace 70 may be selectively adjusted by providing a plurality of shunt lines 84, 94, 96 positioned between the inspiratory hose 54 and the expiratory hose 56, with each shunt line 84,
10 94, 96 being structured with a two-way shunt valve 86, 98, 100. In operation, the amount of deadspace 70 required, as dictated by the size or capacity of the patient, may be selectively provided by using any suitable number of shunt lines 84, 94, 96 to allow exhaled gas to move through the ventilation apparatus 50. For example, given a patient of average size or lung capacity, it may be appropriate to use the
15 first shunt line 84 and the second shunt line 94 as potential deadspace 70. Thus, as the patient exhales in a re-breathing episode, the shunt valves 86, 98 associated with the first shunt line 84 and second shunt line 94 may be opened allowing exhaled and re-breathable gas to fill the expiratory hose 56, the inspiratory hose 54 between the second shunt line 94 and the Y-piece 58, the first shunt line 84 and the second shunt
20 line 94. With a patient of larger size or greater lung capacity, it may be necessary to use the third shunt line 96 as well in providing sufficient deadspace 70 for re-breathing. Notably, each shunt valve 86, 98, 100 may be in electromechanical communication with the computer 76 (not shown in FIG. 7) so that the computer may determine, from the pneumotachometer, for example, that additional deadspace
25 70 is required and cause the opening of one or more of the shunt valves 86, 98, 100 to provide sufficient additional deadspace 70. In an alternative embodiment, the ventilation apparatus 50 shown in FIG. 7 may be modified by the addition of selectively expandable sections 90, as shown in FIG. 6.

In the several alternative embodiments of the invention previously illustrated
30 and described, the amount or volume of the deadspace has been selectively adjustable by providing means for adjusting the volume of the deadspace, such as by providing length expanding means. It may be equally appropriate, however, to provide a change in ventilation, as required by the differential Fick Equation, by

leaking some of the exhaled gas out of the system during the inspiration phase of a breath. Thus, as illustrated by FIG. 8(a), the ventilation apparatus 50 of the present invention may be structured with an evacuation line 106 connected to the expiratory hose 56 of the ventilation apparatus 50. The evacuation line 106 may be structured with gas releasing structure, such as a simple valve 108 connected thereto which, when opened, allows exhaled gas to move through the evacuation line 106. An orifice 110 positioned at the end of the evacuation line 106 allows some of the exhaled gas to escape to the atmosphere.

When and how much exhaled gas should be leaked from the ventilation apparatus 50 during a re-breathing event may be determined by the computer (not shown in FIG. 8) in response to flow conditions, CO₂ conditions and/or the size or lung capacity of the patient. The valve 108, in electromechanical communication with the computer, may be selectively actuated according to ventilation or patient conditions. Where a patient is anesthetized or is otherwise exhaling gas which is undesirable for venting to the atmosphere, a compliant chamber 112, such as an expandable bag shown in FIG. 8(b), may be attached to the evacuation line 106 to receive the exhaled gas leaked from the ventilation circuit.

FIG. 9 schematically illustrates the use of a tracheal gas insufflation (TGI) apparatus 120 to provide the necessary deadspace in determining cardiac output in patients. TGI apparatus is typically used to ventilate sick patients who require the injection of fresh gas into their central airway for the improvement of alveolar ventilation. TGI apparatus can be configured to provide continuous or phasic (e.g., only during inhalation) injections of gas. The TGI apparatus supplies gas, or an oxygen/gas mixture, to the lungs with every breath. As shown in FIG. 9, the TGI apparatus comprises an endotracheal tube 122 which is inserted into the trachea 124 of the patient by intubation procedures. A catheter 126 extends through the endotracheal tube 122 and into the patient's lungs, typically just above the carina. Gas or an oxygen/gas blend is provided from a gas source 128 and is directed through gas tubing 130 into the catheter 126. A flowmeter 132 may assist in determining the optimum amount of gas to be introduced into the lungs.

An adaptor fitting 134 may be used to connect a ventilation circuit 136 of a type previously described to the TGI apparatus 120. That is, a ventilation circuit 136 comprising a Y-piece 58 from which extends an inspiratory hose 54 and an

expiratory hose 56 is structured with a flow meter line 72 attachable to a flow meter (not shown) and a CO₂ sensor 74 for collecting data derived during a re-breathing event. In the illustrated TGI apparatus 120, the endotracheal tube 122 provides deadspace 70 required for re-breathing in addition to the ventilation circuit 136 as previously described. To act as a deadspace, however, the TGI apparatus (i.e., the gas source 128 and flow meter 132) must be turned off, reduced or otherwise disabled. Exhaled air is thereby allowed to fill the endotracheal tube 122 and enter through the Y-piece 58. The endotracheal tube 122 and ventilation circuit 136 serve as deadspace when the TGI apparatus 120 is turned off. The volume of deadspace provided by the TGI apparatus configuration may be further increased or decreased, as necessary, by varying the depth to which the catheter 126 is positioned in the patient's trachea.

The computer to which the flow meter 72 and CO₂ sensor 74 are connected is programmed to receive data collected by the flow meter 72 and CO₂ sensor 74 and to analyze the data to calculate an estimated cardiac output. The parameters which are required by the software program to analyze the data and to estimate cardiac output are described hereafter.

The calculation of cardiac output for a given patient is based on the collection of data from the CO₂ sensor and flow monitor attached to the ventilation apparatus of the present invention. Raw flow and CO₂ signals from the flow monitor and CO₂ sensor are filtered to remove artifacts and the flow signals, CO₂ signals and pressure signals are stored in a buffer in the software program. When the flow signal crosses a prescribed threshold (e.g., 15 liters/minute), the buffer is searched to find the most recent zero-crossing. The zero-crossing is identified as the start of a new breath. All data stored in the buffer since the last zero-crossing and the crossing of the prescribed threshold (i.e., the new zero-crossing) is established as one breathing cycle. For each breathing cycle, the parameters of the breathing phase are calculated as follows:

- 1) **etCO₂**: The average concentration of CO₂ during the final 5% of expiratory tidal volume is taken as end-tidal CO₂.
- 2) **VCO₂**: The integral of flow (in milliliters) multiplied by concentration of CO₂ over the entire breath is VCO₂.

- 3) **Inspired CO₂:** This is the concentration of inspired CO₂. It is the integral of CO₂ concentration times the volume (in milliliters) of air flow during inspiration (i.e., negative flow).
- 4) **Airway deadspace:** Determined as the expired volume (in milliliters) at which CO₂ concentration crosses a selected threshold set at, for example, 0.5 times etCO₂.

The initial values of VCO₂ and etCO₂ are filtered employing a three-point median filter. The etCO₂ and VCO₂ signals are straight-line interpolated and re-sampled at 0.5 Hz.

A correction is made in the VCO₂ value to account for alveolar deadspace. That is, the correction in VCO₂ corrects for the flow of CO₂ into lung stores such as the functional residual capacity (FRC) in the lungs, or, in other words, the volume of gas left in the lungs at the end of a breath. Alveolar deadspace is demonstrated more clearly in FIG. 10, which schematically illustrates the lungs 150 of a patient. The lungs 150 generally comprise the trachea 152, bronchi 154 and alveoli 156. The trachea 152 and bronchi 154 generally comprise what is known as the anatomic or serial deadspace, which exists in the region indicated between arrows A and B. In the lungs 150, there are alveoli 156 which are perfused with blood (i.e., in contact with blood flow to provide oxygenation to the blood) and alveoli which are not perfused, though both perfused and un-perfused alveoli 156 may be ventilated.

Perfused alveoli 160 and unperfused alveoli 162 are illustrated in FIG. 10. The perfused alveoli 160 are contacted with blood flowing through minute capillaries 164 surrounding the alveoli 160, the venous blood 166 flowing toward the alveoli 160 and the arterial blood 168 flowing away from the alveoli 160 in the direction of arrow 170. In the alveoli 160, 180, a volume of gas, known as the functional residual capacity (FRC) 172 remains in the alveoli following exhalation. A portion 172 of the alveoli 160 which is evacuated upon exhalation (i.e., is ventilated) is representational of alveolar CO₂ (PA_{CO₂}). In un-perfused alveoli 162, the FRC 176 contains gas which is not evacuated during a breath, and the ventilated portion 178 of the alveoli 162 forms a space containing gas or CO₂ which is ventilated, but not perfused. It is the ventilated portion 178 existing in the un-

perfused alveoli 162 which comprises parallel deadspace (PDS), so called because it is ventilated in parallel with the perfused alveoli.

In the present invention, the software program compensates, or accounts, for the functional residual capacity of the patient's lungs and the alveolar deadspace
5 which exists. The correction is equal to the FRC times the change in end tidal concentration or

$$VCO_2 = VCO_2 + FRC \times \Delta etCO_2 / Pbar,$$

where "Pbar" is barometric pressure. FRC is estimated as a function of body weight as estimated by the deadspace volume using the equation

10
$$FRC = FRC\text{-factor} \times \text{airway deadspace} + \text{an off-set value},$$

where the FRC-factor is a value experimentally determined or is based on published data known in the art and the off-set value is a fixed constant which is added to compensate for breathing masks or other equipment components which may add deadspace to the circuit and thereby unacceptably skew the relationship between
15 FRC and deadspace. The airway deadspace is the volume at which CO₂ crosses a selected threshold [e.g., 0.5etCO₂]. Dry gas is assumed in all equations.

Compensation is also made for parallel deadspace (See FIG. 10). Parallel dead space CO₂ concentration is calculated as a low pass filtered version of the mixed inspired CO₂ plus the airway deadspace times the previous end tidal CO₂
20 concentration. The average CO_{2PDS} is etCO₂ times airway deadspace plus inspired CO₂ volume divided by the tidal volume. Breath-by-breath calculation of parallel deadspace, or unperfused space, concentration is therefore:

$$CO_{2PDS}(n) = [FRC / (FRC + V_t)] \times CO_{2PDS}(n-1) + ([V_{iCO_2} + \text{deadspace} \times etCO_2(n-1)] / V_t) \times [V_t / (V_t + FRC)]$$

25 where V_t is the tidal volume (the volume of the breath), PDS is parallel deadspace (i.e., space in the lung that is ventilated but not perfused by blood flow), etCO₂ is the concentration of CO₂ at the end of the exhaled breath, or "end-tidal," "dead space" is the volume in the trachea and bronchi through which air must pass to get to the alveoli but in which no gas exchange occurs (also defined as "serial dead
30 space," See FIG. 10) and (n-1) indicates the previous breath.

Alveolar CO₂ partial pressure ("PA_{CO₂}") is calculated from the end-tidal CO₂ and the CO₂ in the parallel deadspace. Thus, if

$$etCO_2 = r \times PA_{CO_2} + (1-r)PDS_{CO_2},$$

then

$$PA_{CO_2} = [etCO_2 - (1-r)PDS_{CO_2}] / r,$$

- 5 where r is the perfusion ratio calculated as the ratio of perfused alveolar ventilation divided by total alveolar ventilation, or $(V_A - V_{PDS}) / V_A$. The perfusion ratio r is estimated to be about 0.92. Perfusion ratio can also be estimated by direct analysis of arterial blood.

The PA_{CO_2} signal is then converted to CO_2 content using the following equation:

10
$$C_{CO_2} = (6.957 \times Hb + 94.864) \times \ln(1 + 0.1933(P_{CO_2})),$$

where C_{CO_2} is the concentration of CO_2 and Hb is hemoglobin concentration. In some instances, a hemoglobin count may be readily available and is used in the equation. If hemoglobin (Hb) concentration is not available, the value of 11.0 is used in the software program.

- 15 Baseline values of $etCO_2$ and VCO_2 , also referred to herein as "before CO_2 and before VCO_2 ," are those values which exist during normal breathing and are calculated as the average of all samples between 27 and 0 seconds before the start of re-breathing. Once a re-breathing episode begins, the VCO_2 value during re-breathing, also referred to herein as "during VCO_2 ," is calculated as the average
- 20 VCO_2 between 25 and 30 seconds of re-breathing. The calculation of C_{CO_2} during a re-breathing episode is determined using a regression line to predict the stable concentration of alveolar CO_2 (C_{CO_2}). To predict the C_{CO_2} at which the signal will be stable (i.e., unchanging) the C_{CO_2} is plotted versus the breath-to-breath change in concentration. The line is regressed and the intersection between the C_{CO_2} and zero

- 25 ΔC_{CO_2} is the predicted stable point.

Cardiac output is then calculated as follows:

$$CO_2 = [before V_{CO_2} - during V_{CO_2}] / [during C_{CO_2} - before C_{CO_2}].$$

The operation logic of the software program is briefly illustrated in the flow chart of FIG. 11. The computer is programmed to detect the end of an exhalation 200 at which point the computer collects data from the CO₂ sensor and the flow meter and calculates CO₂, VCO₂, Inspired CO₂ and airway deadspace values 202.

5 The program then calculates FRC, at 204, according to the equation previously noted. The program also corrects the VCO₂ value, at 206, in accordance with the equation previously described. At thirty second intervals (thirty seconds only being an average time, which may be adjusted higher or lower commensurate with the size of the patient), the CO₂ and VCO₂ values are re-calculated, at 210, to provide
10 an average of those values based on time, not on the variable time at which exhalation may end.

The program then calculates the estimated pCO₂ in the parallel deadspace 212 and calculates the estimated pCO₂ in the alveoli 214 using the equations previously described. At that point, a re-breathing episode is initiated 216 and a
15 deadspace is introduced. Again, the computer collects data from the CO₂ sensor and the flow monitor of the apparatus and from that data, the change in VCO₂ and alveolar CO₂ induced by the introduction of the deadspace is calculated 218. If the calculated change in VCO₂ is less than twenty percent (20%) of the baseline VCO₂ or if the change in partial pressure of alveolar CO₂ is less than 3mm Hg 220, then
20 the operator is notified to increase the partial re-breathing deadspace 222 by increasing the expandable volumetric dimension of the adjustable deadspace of the apparatus. Baseline values are cancelled 224 then recalculated, as suggested by arrow 226. If, however, the change in VCO₂ during re-breathing is greater than 80% of baseline values, then the operator is notified to decrease the adjustable
25 deadspace of the apparatus by decreasing the volumetric dimension of the adjustable deadspace 230. The baseline values are cancelled 232 and recalculated, as suggested by arrow 234. Notably, the computer may notify the operator to make the necessary changes in the adjustable deadspace or, in an alternative embodiment, the computer may signal mechanical means connected to the adjustable deadspace to
30 increase or decrease the volumetric dimension of the deadspace automatically.

Upon proper adjustment of the adjustable deadspace and the recalculation of baseline CO₂, VCO₂, inspired CO₂ and airway deadspace values, the alveolar partial pressure (etCO₂) is converted by the software program to CO₂ content and the

change in CO_2 content induced by the introduction of deadspace in the re-breathing episode is calculated 236. From those values, cardiac output is calculated 238 in accordance with the equation previously described.

5 All references to times of data collection assume a thirty (30) second re-breathing period. However, the actual length of time for periods of re-breathing are dependent upon the patient's size, lung capacity and cardiac output determined from previous breathing cycles. The program also controls the operation of the shunt valve or valves in the re-breathing apparatus. The valve or valves are opened based on a timer value determined by patient size, capacity and/or cardiac output.

10 The ventilation apparatus of the present invention provides a new and more accurate means of determining cardiac output in patients. The structure and electronic capabilities of the present invention may be modified, however, to meet the demands of the particular application. Hence, reference herein to specific details of the illustrated embodiments is by way of example and not by way of
15 limitation. It will be apparent to those skilled in the art that many additions, deletions and modifications to the illustrated embodiments of the invention may be made without departing from the spirit and scope of the invention as defined by the following claims.

CLAIMSWhat is claimed is:

1. Apparatus for non-invasive determination of cardiac output comprising:
 - 5 an airway conduit for contact with a patient's airway;
 - an inspiratory conduit interconnected to said airway conduit;
 - an expiratory conduit interconnected to said airway conduit;
 - a volume-adjustable deadspace positioned in fluid communication with said expiratory conduit; and
 - 10 detection apparatus positioned in proximity to said airway conduit for detecting changes in gas concentrations and gas flow from said patient.
2. The apparatus of claim 1 wherein said volume-adjustable deadspace includes at least one shunt line extending between said expiratory conduit and said
15 inspiratory conduit, said shunt line being structured with a selectively actuated shunt valve providing movement of exhaled gas between said inspiratory conduit and said expiratory conduit via said shunt line.
3. The apparatus of claim 2 further comprising a source of ventilation in
20 communication with said airway conduit to provide gas to a patient.
4. The apparatus of claim 2 further comprising a plurality of shunt lines extending between said expiratory conduit and said inspiratory conduit, each said shunt line having a selectively actuated shunt valve providing movement of exhaled
25 gas between said inspiratory conduit and said expiratory conduit.
5. The apparatus of claim 2 wherein said expiratory conduit includes a volume-expandable section and said inspiratory conduit includes a volume-expandable section, each said volume-expandable section being positioned to
30 selectively expand said volume-adjustable deadspace.
6. The apparatus of claim 5 further comprising a source of ventilation in communication with said airway conduit to provide gas to a patient.

7. The apparatus of claim 5 further comprising a plurality of shunt lines extending between said expiratory conduit and said inspiratory conduit, each said shunt line having a selectively actuated shunt valve providing movement of exhaled gas between said inspiratory conduit and said expiratory conduit.

5

8. The apparatus of claim 1 wherein said volume-adjustable deadspace is a length of conduit positioned between said airway conduit and said expiratory conduit.

10

9. The apparatus of claim 8 wherein said length of conduit is structured with a volume-expandable section.

10. The apparatus of claim 9 further comprising a three-way valve for selectively directing gas through said length of conduit.

15

11. The apparatus of claim 8 further comprising a source of ventilation in communication with said airway conduit to provide gas to a patient.

12. The apparatus of claim 9 wherein said length of conduit further comprises an inlet, an outlet and a restrictor valve positioned therebetween for selectively preventing flow of gas into said volume-adjustable deadspace, and further comprising a two-way valve positioned in proximity to said volume-adjustable deadspace and said expiratory conduit for selectively directing gas through said volume-adjustable deadspace.

25

13. The apparatus of claim 12 further comprising a source of ventilation in communication with said airway conduit to provide gas to a patient.

14. The apparatus of claim 1 wherein said adjustable deadspace is a selectively length-expandable section positioned between said airway conduit and said expiratory conduit and a selectively length-expandable section positioned between said airway conduit and said inspiratory conduit.

30

15. The apparatus of claim 1 wherein said adjustable deadspace is an expandable section of conduit positioned between said airway conduit and a source of ventilation gas.

5 16. The apparatus of claim 1 wherein said volume-adjustable deadspace includes an evacuation line connected to said expiratory conduit, said evacuation line having gas releasing structure for evacuating gas from said evacuation line for reducing the volume of said deadspace.

10 17. The apparatus of claim 16 further comprising a compliant receptacle attached to said evacuation line for receiving evacuated exhaled gas therein.

18. The apparatus of claim 1 wherein said volume-adjustable deadspace is provided by a tracheal gas insufflation device.

15

19. Apparatus for non-invasively determining cardiac output of a patient comprising an airway conduit for contact with a patient's airway, an inspiratory conduit connected to said airway conduit and an expiratory conduit connected to said airway conduit, said expiratory conduit being structured with an evacuation line
20 for selectively evacuating an amount of exhaled gas from said patient and a selectively-adjustable valve connected to said evacuation line for releasing an amount of exhaled gas through said evacuation line.

20. The apparatus of claim 19 further comprising an evacuation port for
25 releasing gas, and further comprising a compliant receptacle connected thereto for receiving said exhaled gas.

21. The apparatus of claim 19 further comprising a source of ventilation in communication with said airway conduit to provide gas to a patient.
30

22. Apparatus for non-invasively determining cardiac output of a patient comprising an airway conduit for contact with a patient's airway, a source of gas in communication with said airway conduit, a gas insufflation conduit extending from

said source of gas to said patient's lungs and positioned in tandem with said airway conduit to directly deliver gas to a patient's lungs for insufflation thereof, a source of ventilation connected to said airway conduit for providing gas thereto, an inspiratory conduit interconnected between said source of ventilation and said
5 airway conduit and an expiratory conduit interconnected between said source of ventilation and said airway conduit, said gas insufflation conduit and airway conduit being sized and positioned to provide an intermittent deadspace from which a patient can re-breathe exhaled gas.

- 10 23. A method for non-invasively measuring cardiac output comprising:
providing ventilation apparatus for measuring pulmonary gas output of a patient,
said apparatus including an airway conduit for contact with a patient's
trachea, an inspiratory tube connected to said airway conduit, an expiratory
tube connected to said airway conduit and a deadspace connected to said
15 airway conduit;
connecting said airway conduit to a patient's trachea to provide ingress and egress
of air therethrough;
initiating normal breathing in the patient;
measuring the volume of gas and end-tidal gas concentration for a selected period of
20 ventilation to establish a baseline gas concentration and gas volume output;
calculating the end-tidal concentration of gas and calculating the concentration of
gas over the period of one inhalation and one exhalation;
calculating the concentration of gas during exhalation and calculating anatomic
deadspace;
25 redetermining the value of concentration of gas over the period of one inhalation
and one exhalation to account for alveolar deadspace;
redetermining the gas concentrations to adjust for parallel deadspace;
introducing a change in ventilation by directing exhaled gas from the patient into
said deadspace for re-breathing by the patient;
30 measuring the change in gas volume and gas concentration during an episode of re-
breathing;
repeating said normal breathing and measuring of said volume of gas and end-tidal
gas concentration, and recalculating said values of end-tidal gas

concentration, gas concentration over inhalation and exhalation and gas concentration during inspiration;
redetermining said gas concentration to account for parallel deadspace; and
calculating the difference between said baseline gas concentrations and volume of
5 gas output with the detected change in gas concentration and gas volume output following re-breathing.

24. The method according to claim 23 wherein said dead space of said ventilation apparatus is volume-adjustable, said method further comprising:
10 adjusting said volume-adjustable deadspace of said ventilation apparatus responsive to a perceived variance from a selected value of gas concentration per volume of gas prior to repeating said normal breathing.

25. The method according to claim 24 wherein said measured gas is CO₂
15 expelled from said lungs of said patient.

26. The method according to claim 25 wherein said adjusting of said volume-adjustable deadspace comprises expanding the volume of said deadspace responsive to a perceived value of expelled gas volume less than twenty percent of
20 said baseline value of expelled gas volume.

27. The method according to claim 25 wherein said adjusting of said volume-adjustable deadspace comprises expanding the volume of said deadspace responsive to a perceived change in value of said alveolar gas concentration less
25 than 3mm Hg partial pressure.

28. The method according to claim 25 wherein said adjusting of said volume-adjustable deadspace comprises decreasing the volume of said deadspace responsive to a perceived value of greater than eighty percent of said baseline
30 expelled gas volume.

29. The method according to claim 25 wherein said adjusting of said volume-adjustable deadspace comprises evacuating a portion of said exhaled re-breathed gas from said deadspace.

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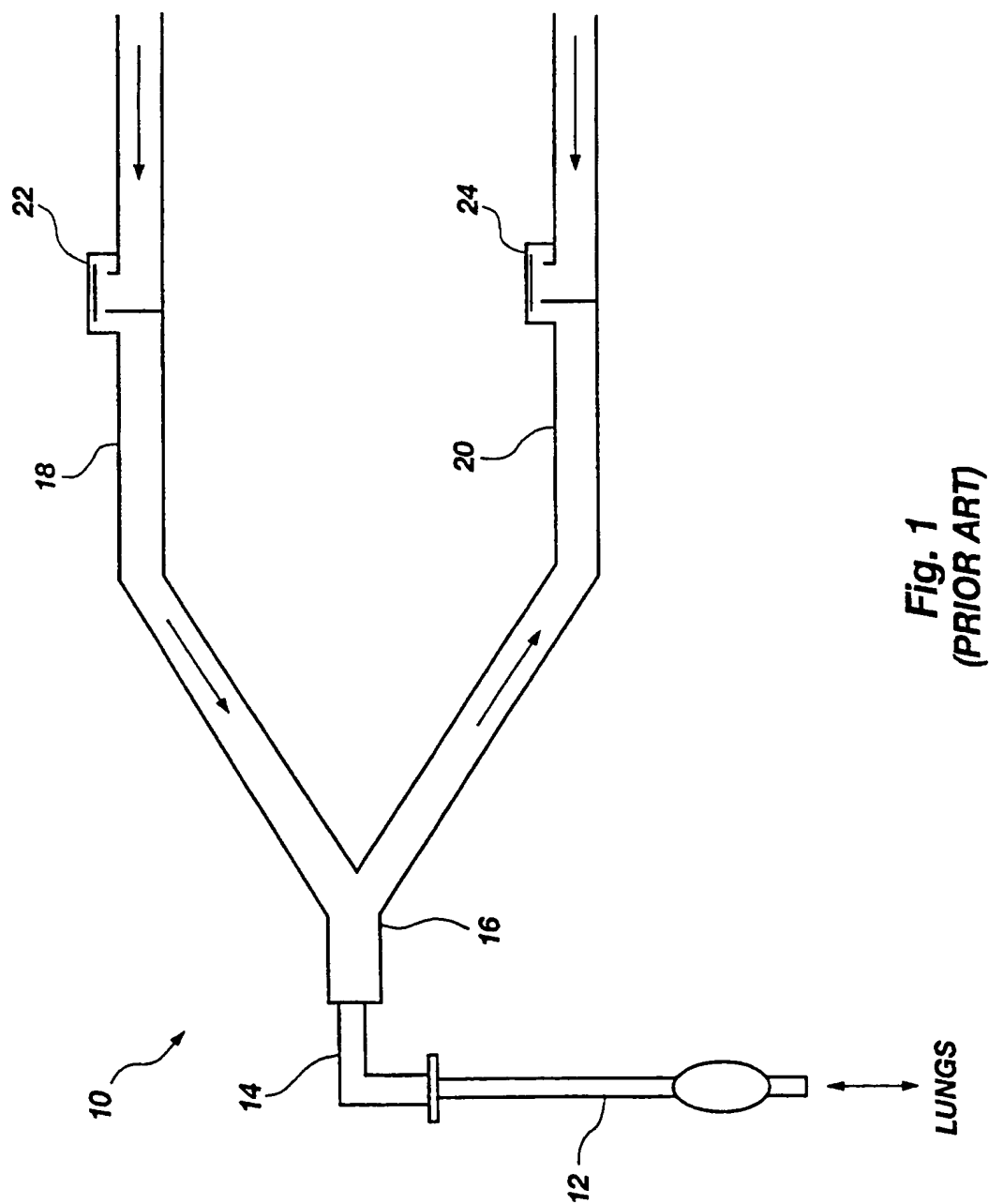


Fig. 1
(PRIOR ART)

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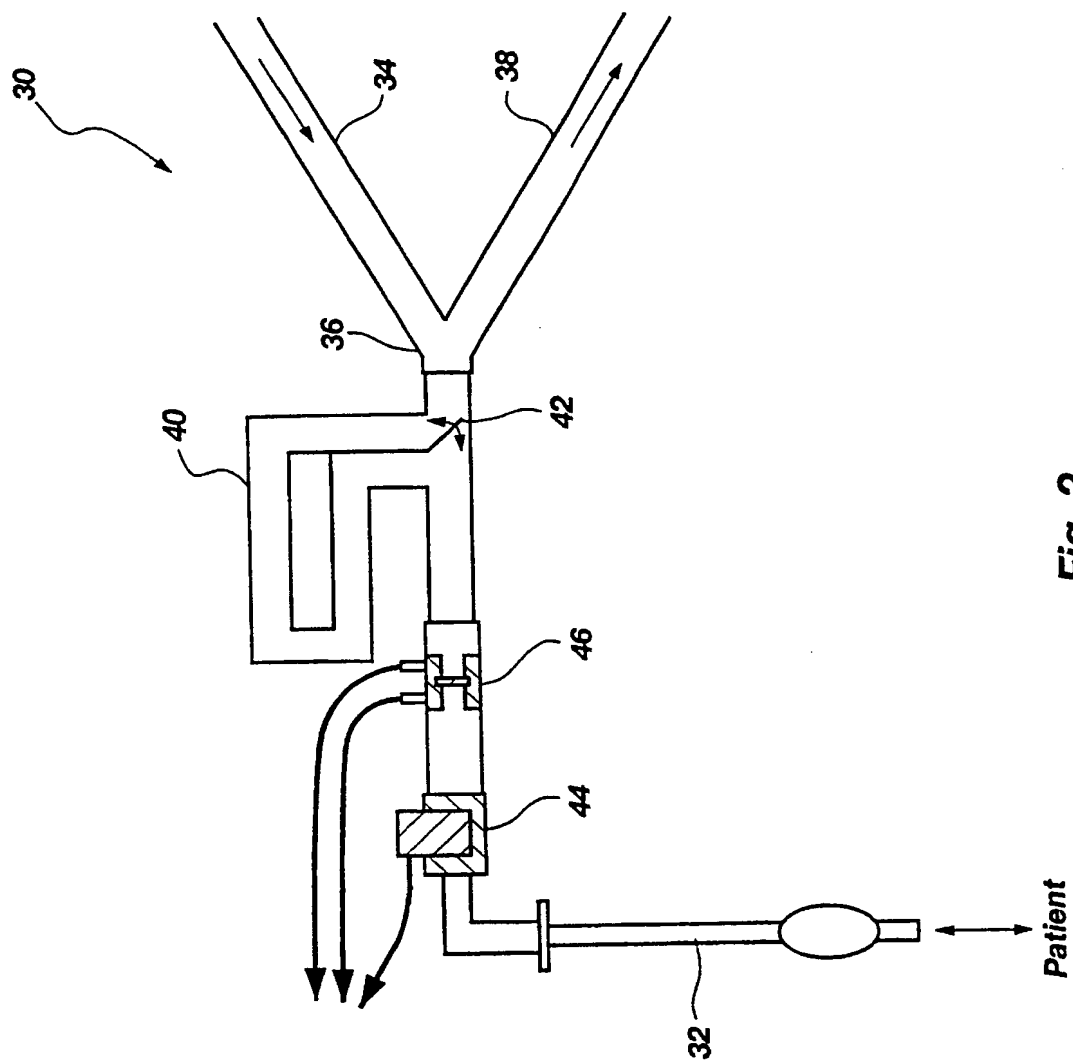


Fig. 2
(PRIOR ART)

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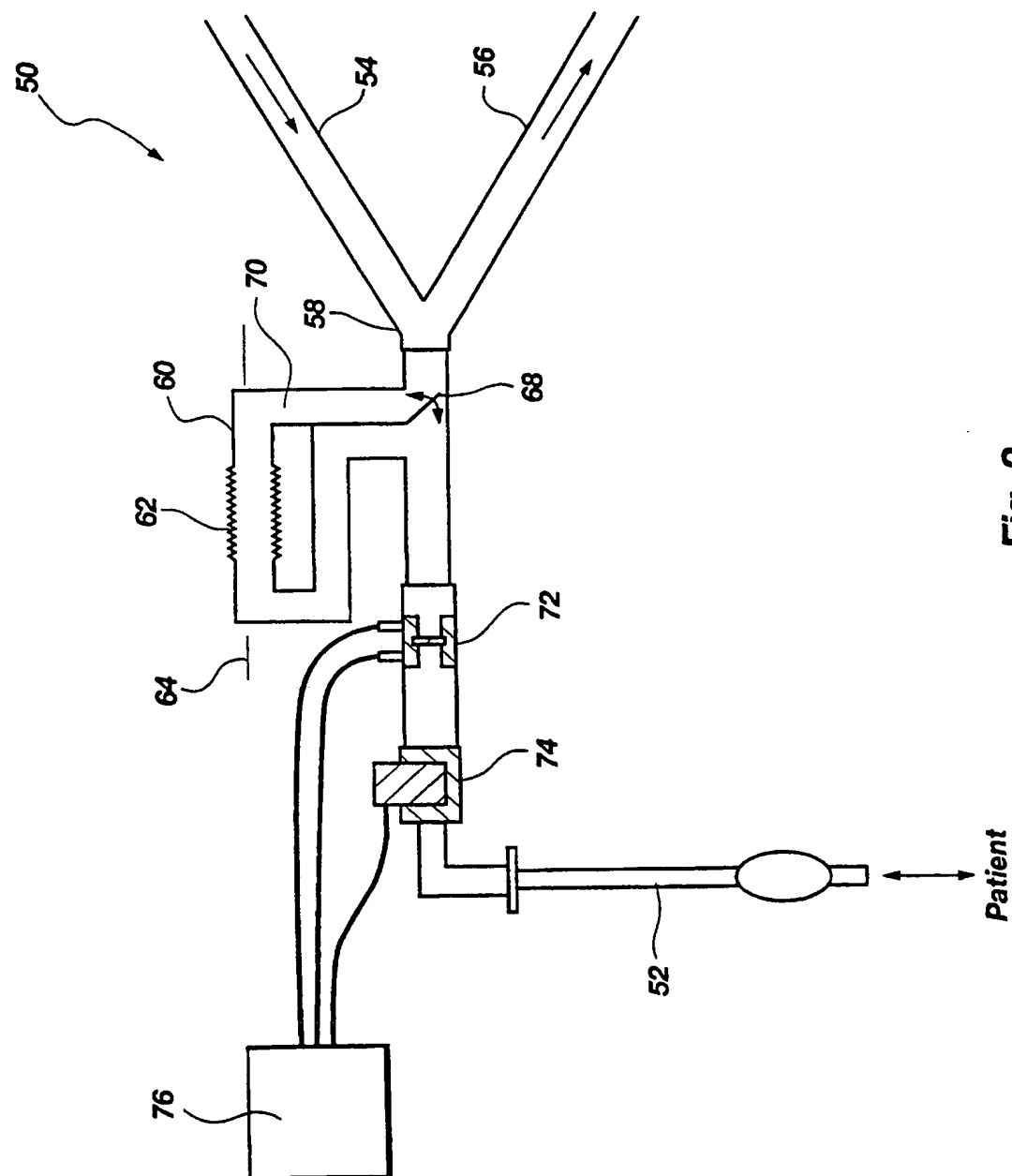


Fig. 3

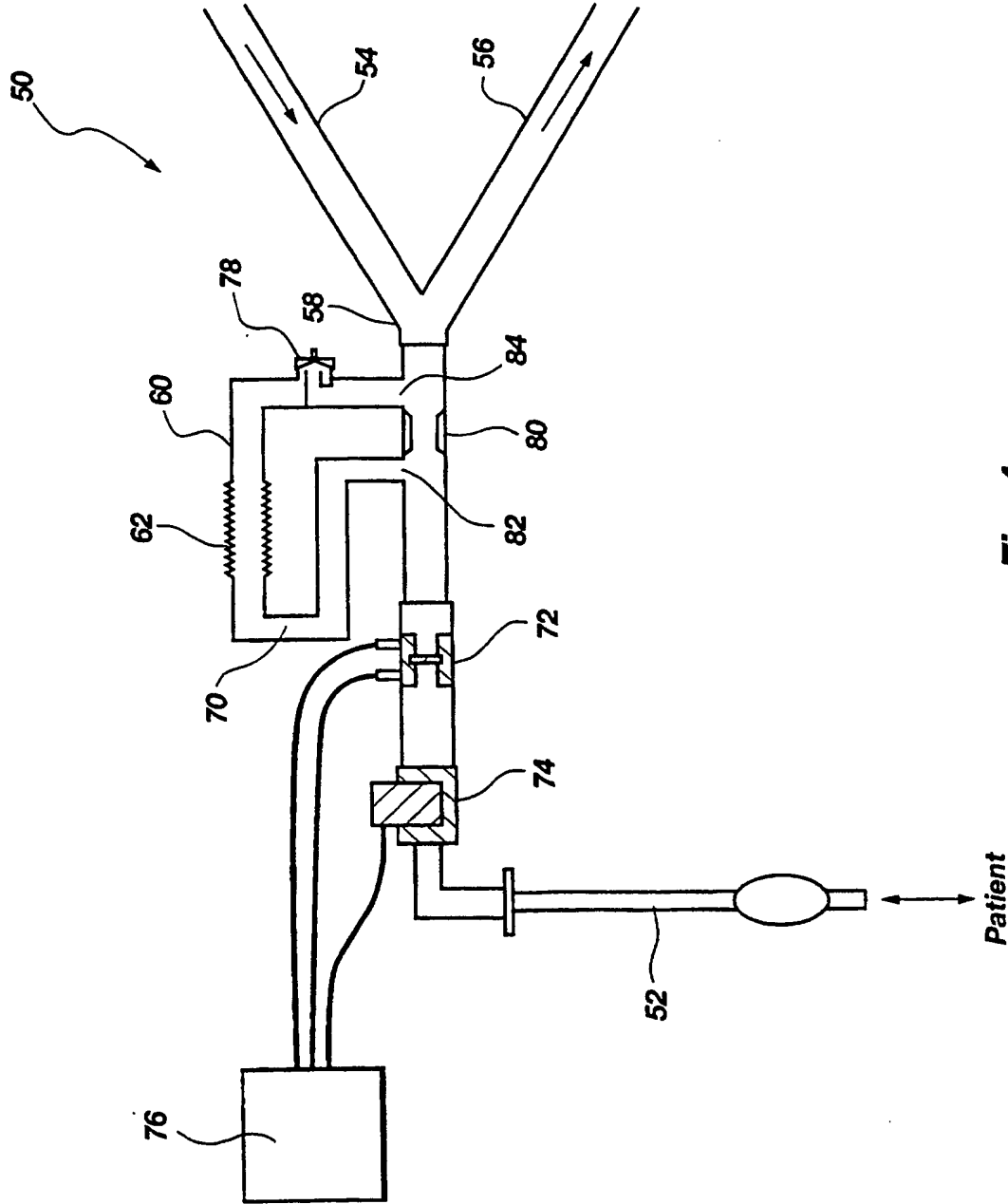


Fig. 4

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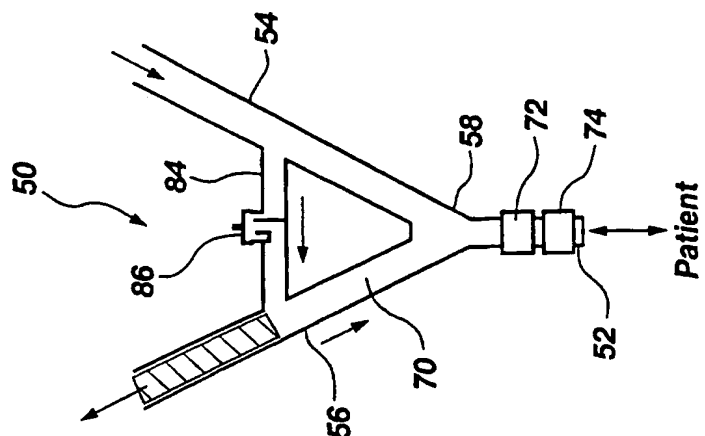


Fig. 5C

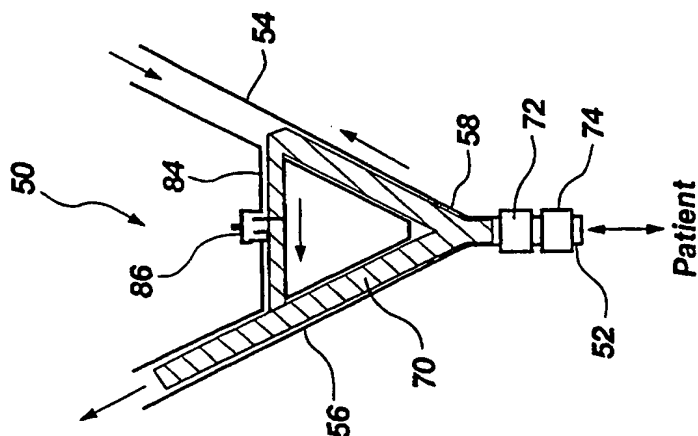


Fig. 5B

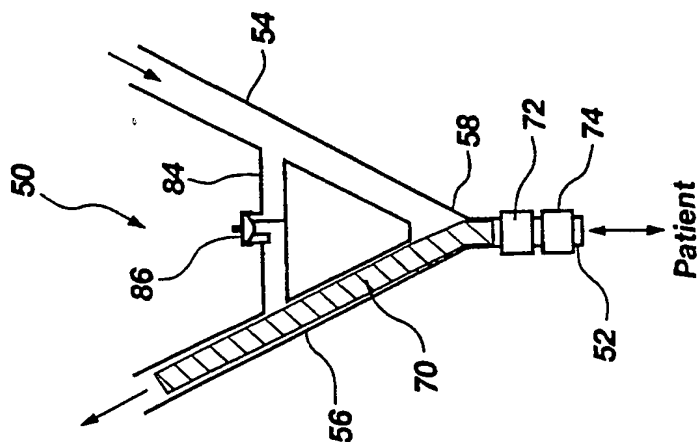


Fig. 5A

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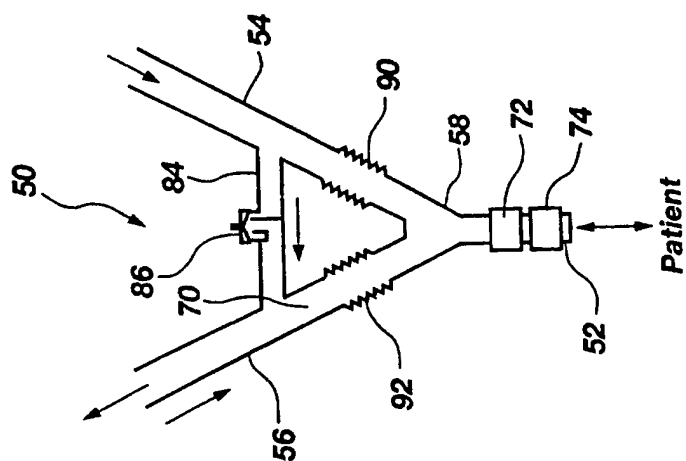
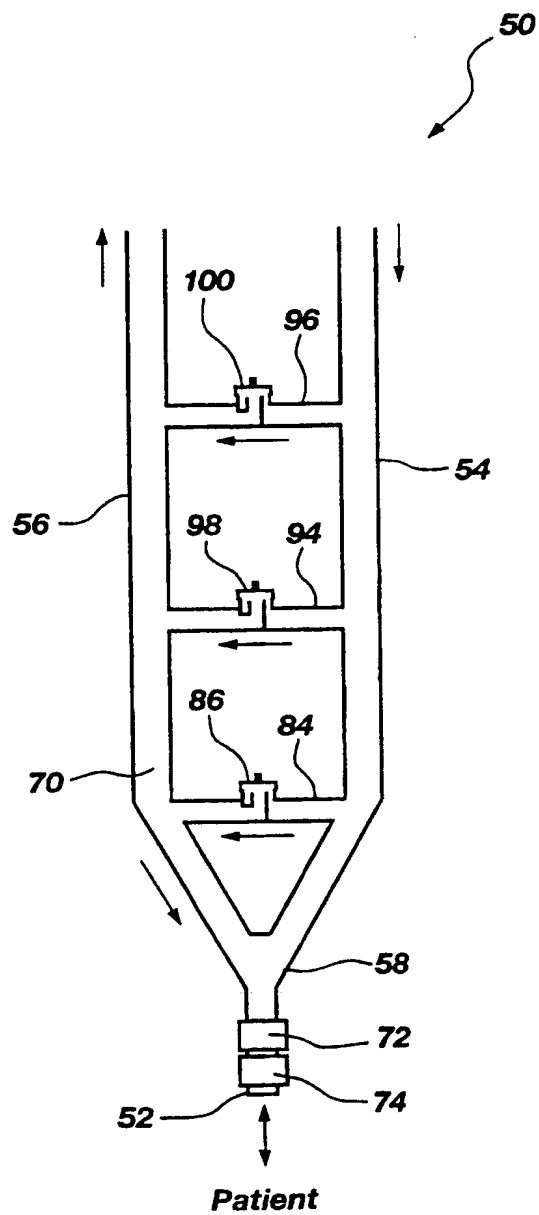
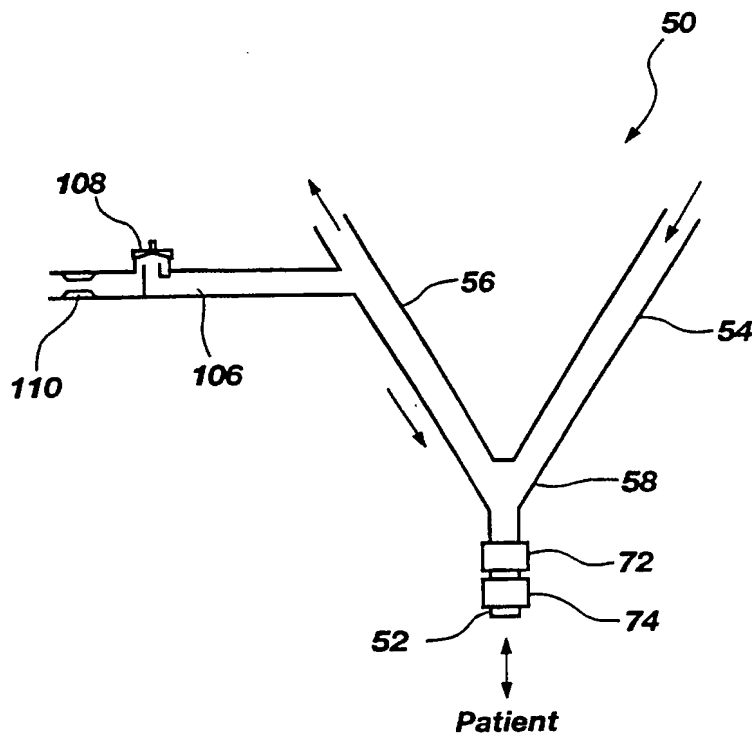
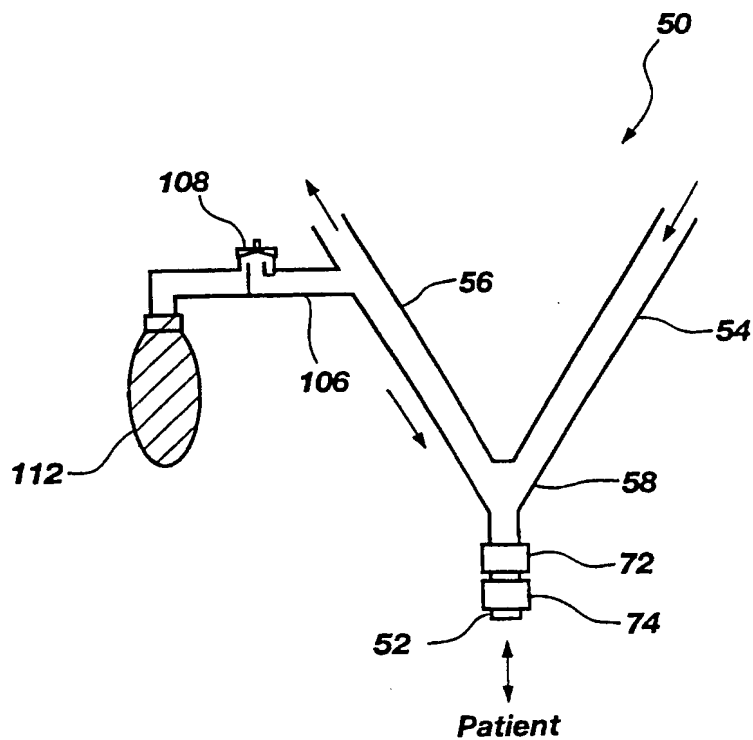


Fig. 6

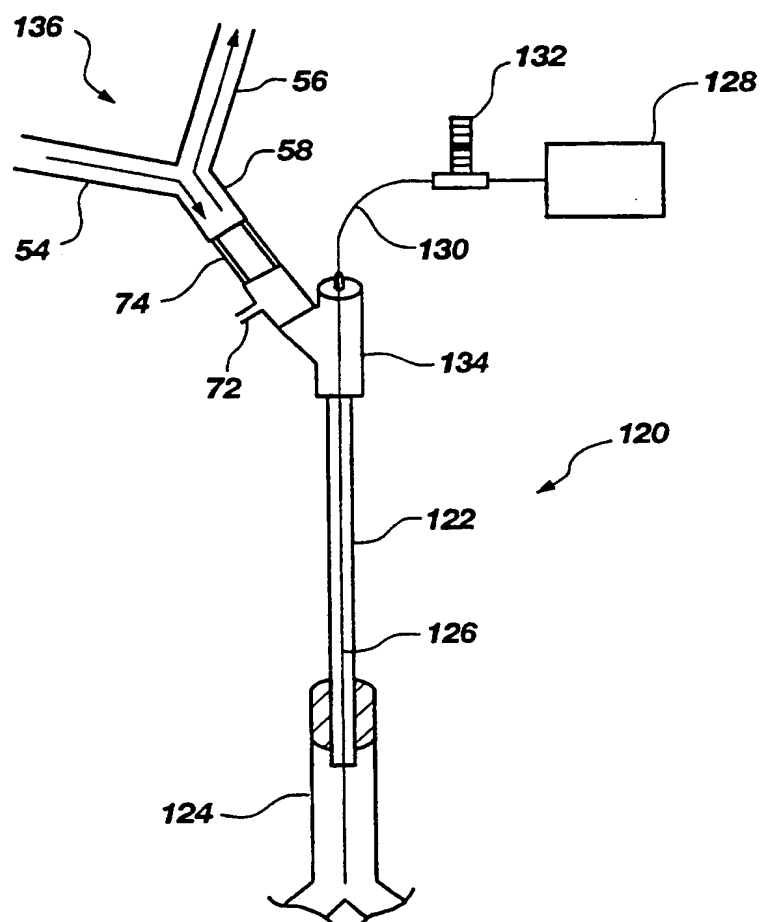
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**Fig. 7**

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**Fig. 8A****Fig. 8B**

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**Fig. 9**

10/11

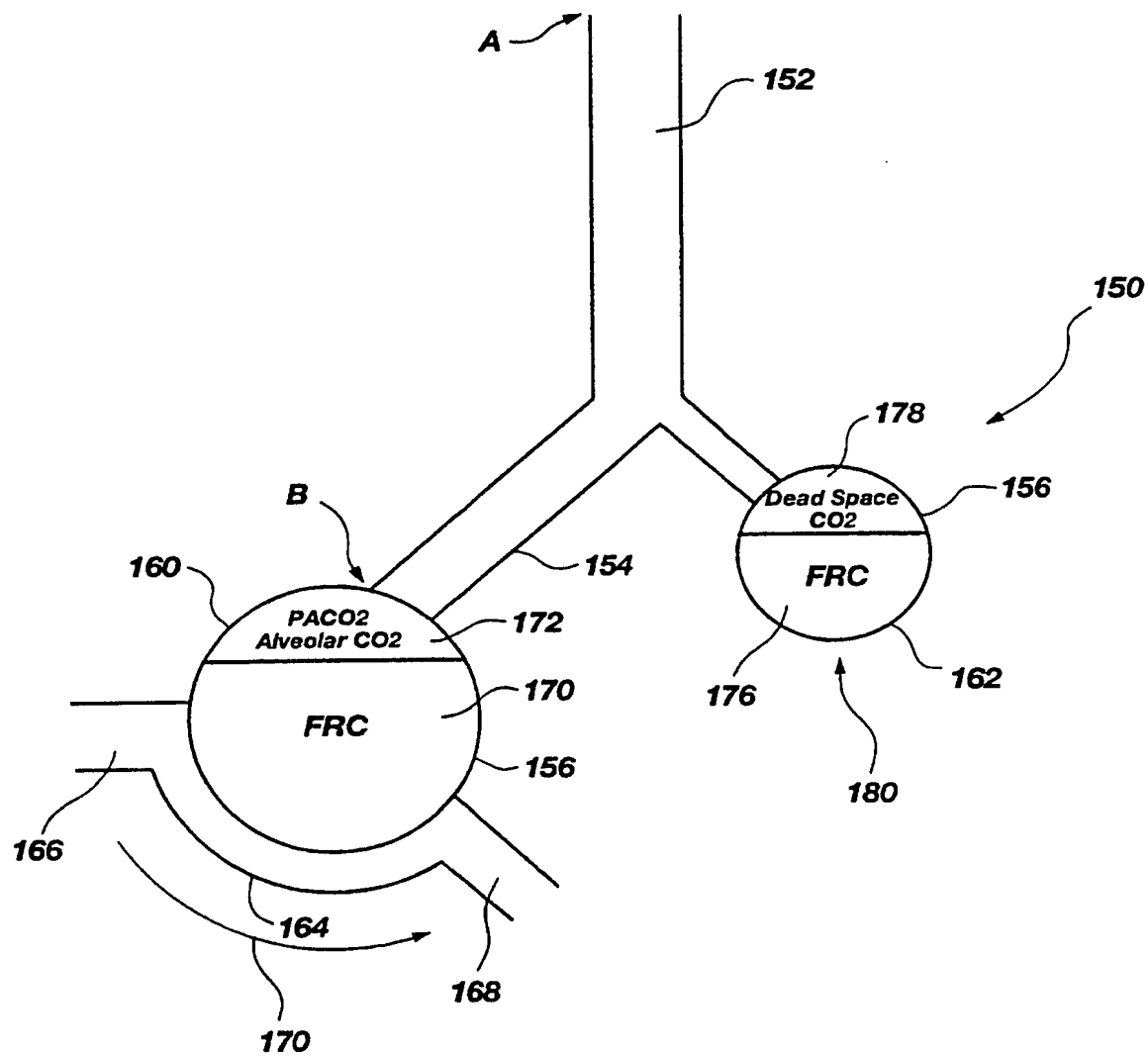


Fig. 10

11/11

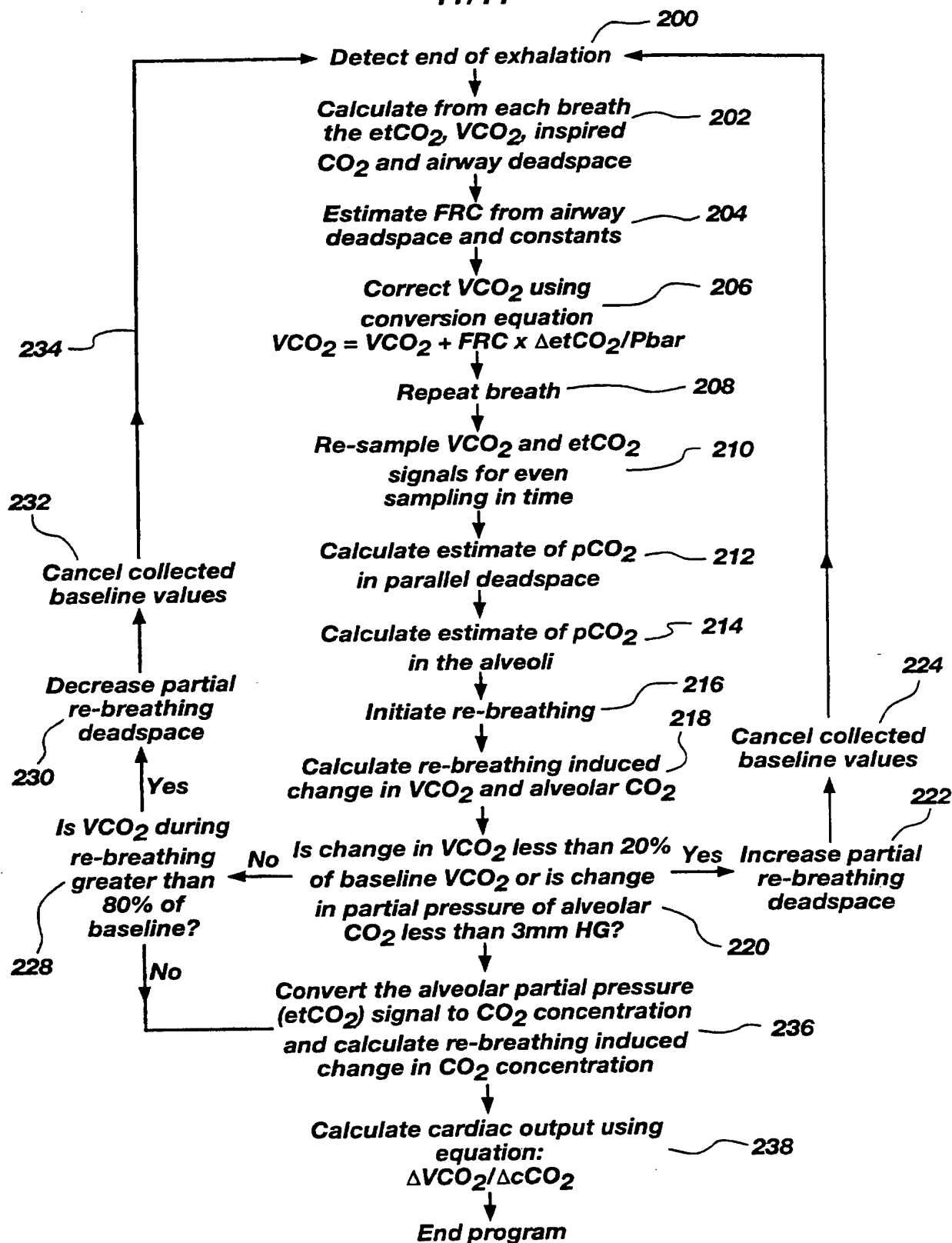


Fig. 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/24263

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/200.26,207.14,207.15, 207.16 ; 600/483,484,485,481,529,532,531,543

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
noneElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
none

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,642,726 A (OWENS ET AL.) 01 JULY 1997, ABSTRACT, COL. 3, L 50+, COL. 4, L 1-15, COL. 2, L 42+, COL. 3, L 45-55	1-16
Y	US 3,910,261 A (RAGSDALE ET AL.) 07 OCTOBER 1975, ABSTRACT, COL. 1, LINES 1-10, LINES 23-35, LINES 52-62.	1-16



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

27 MARCH 1998

Date of mailing of the international search report

21 APR 1998

Name and mailing address of the ISA/US
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/24263

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61B 5/00

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

128/200.26,207.14,207.15, 207.16 ; 600/483,484,485,481,529,532,531,543

1/11

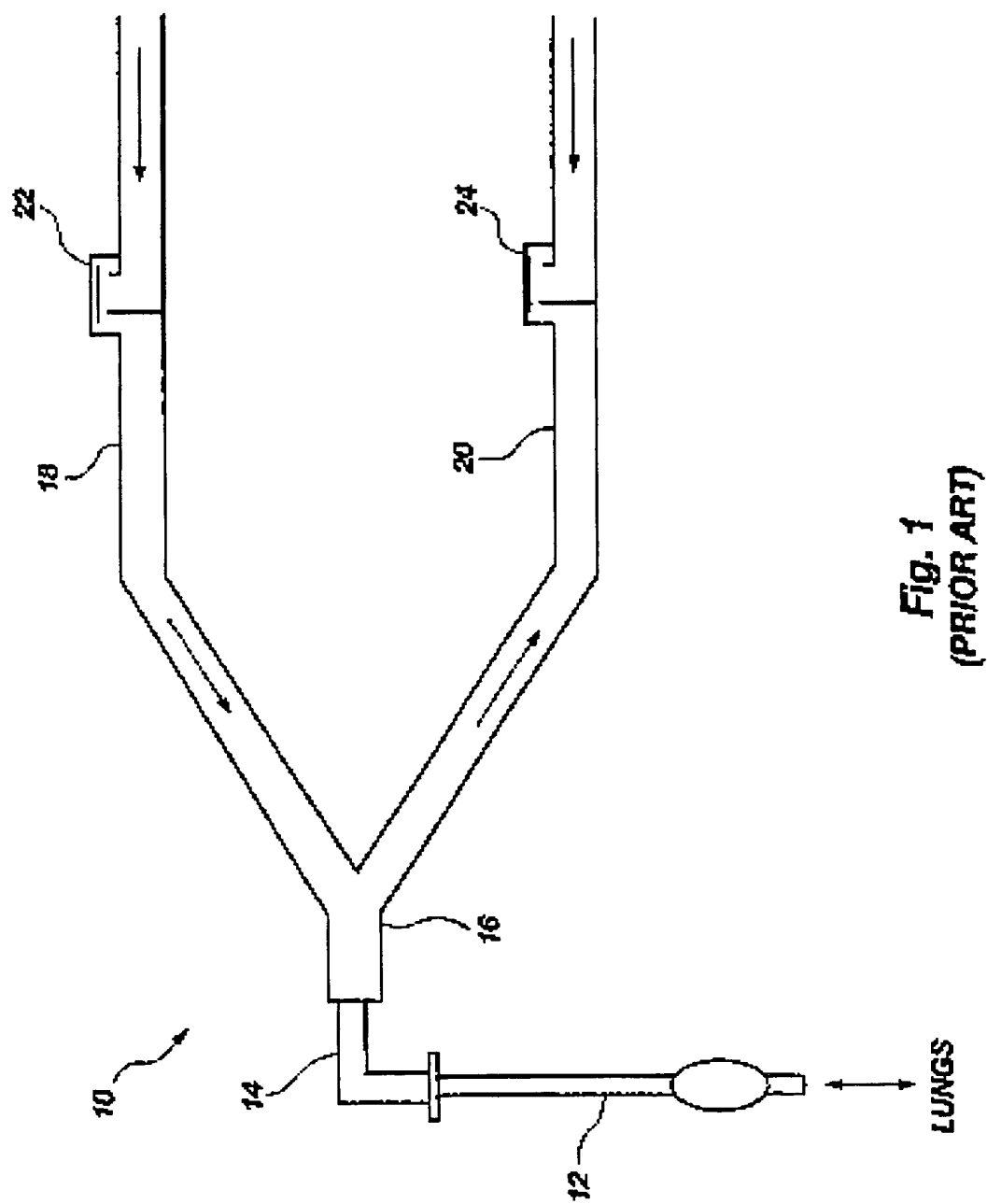


Fig. 1
(PRIOR ART)

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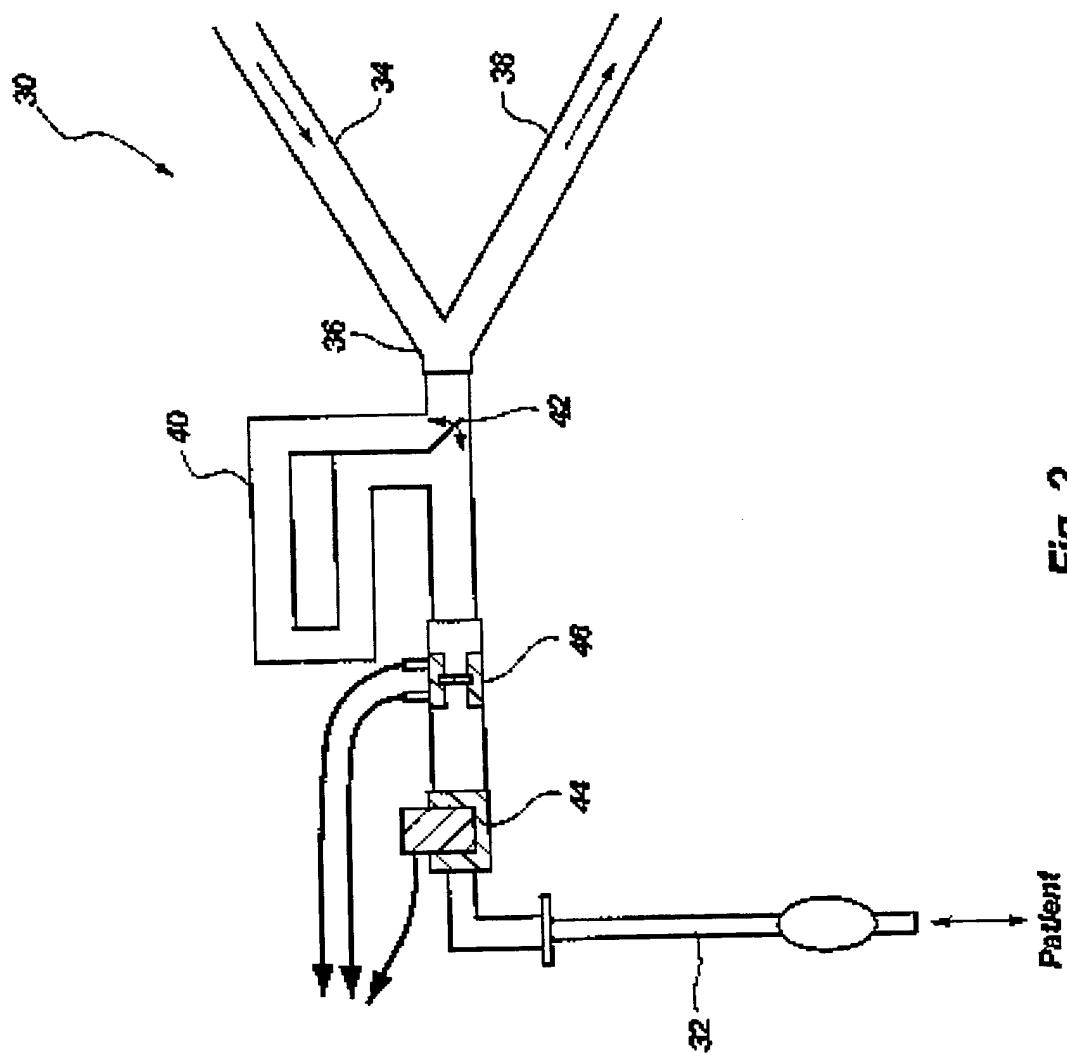


Fig. 2
(PRIOR ART)

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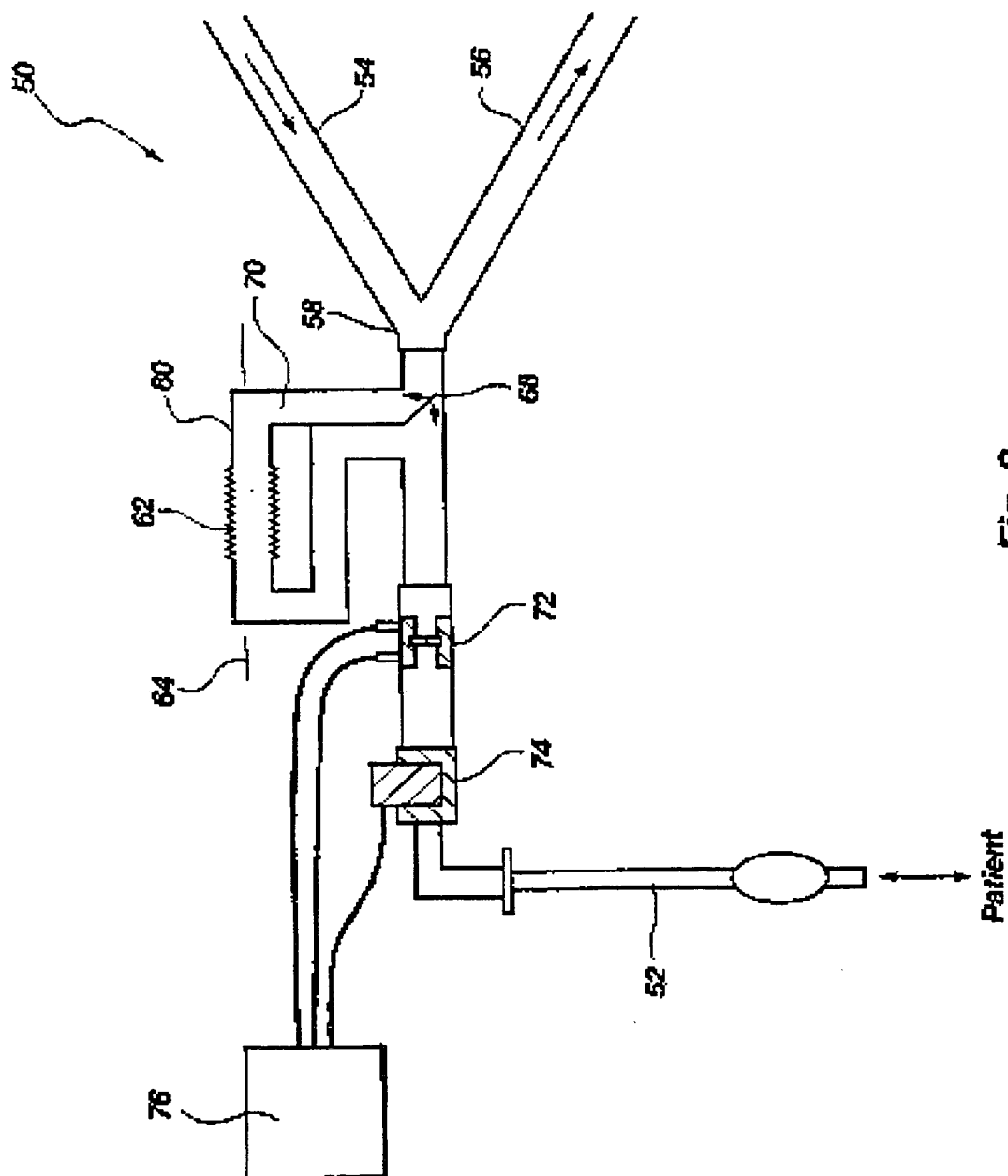
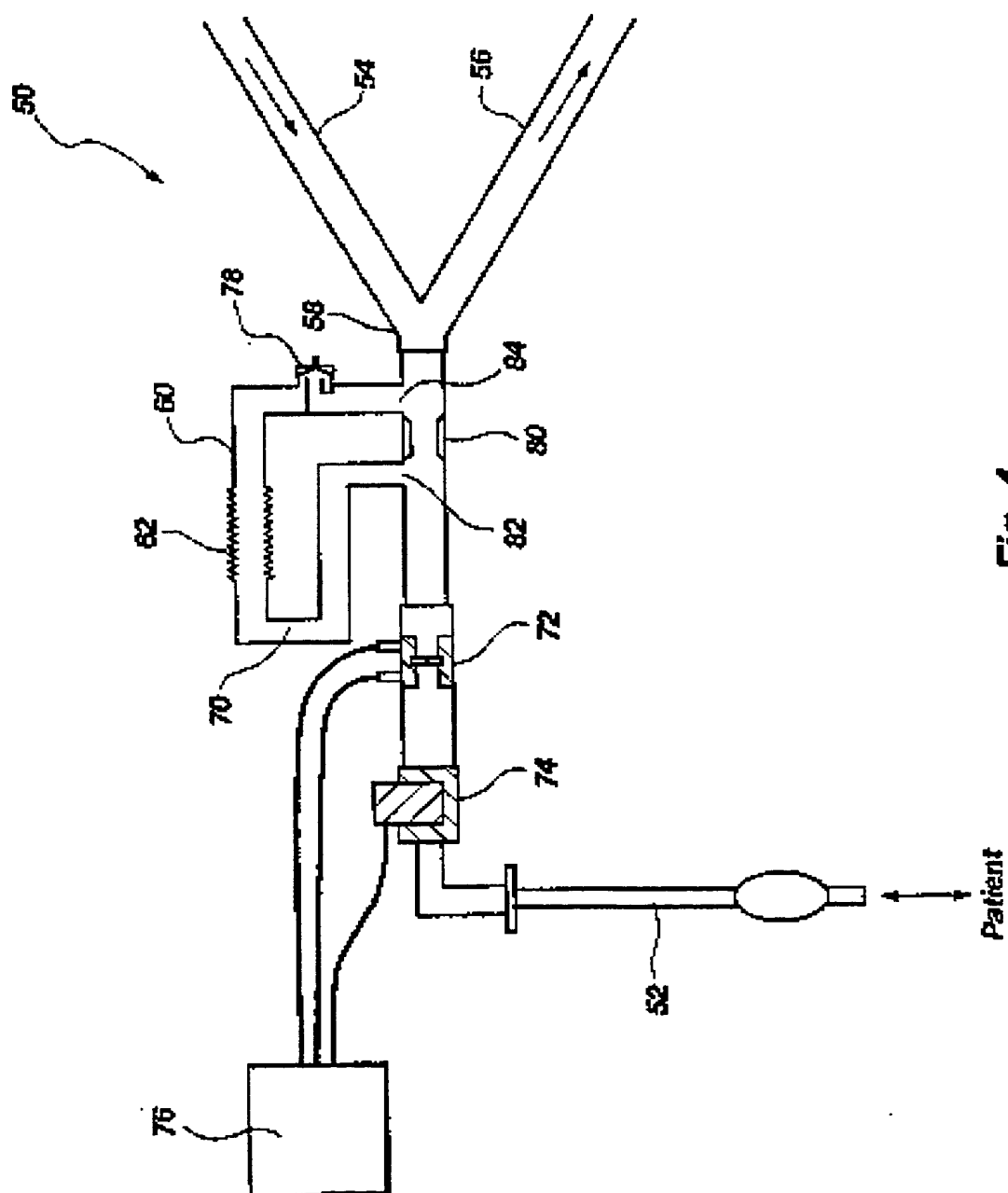


Fig. 3

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Patient

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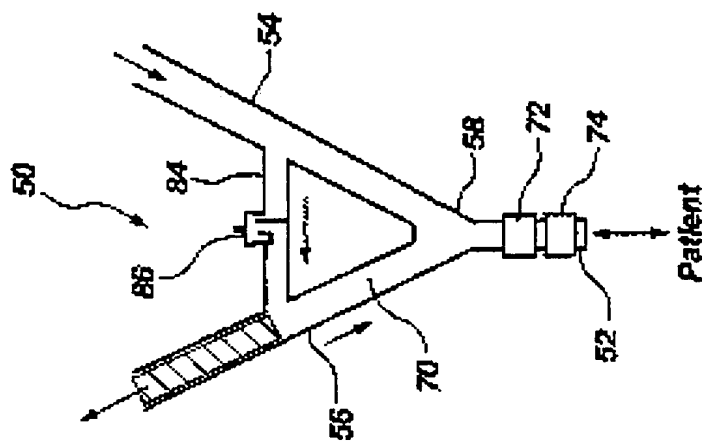


Fig. 5C

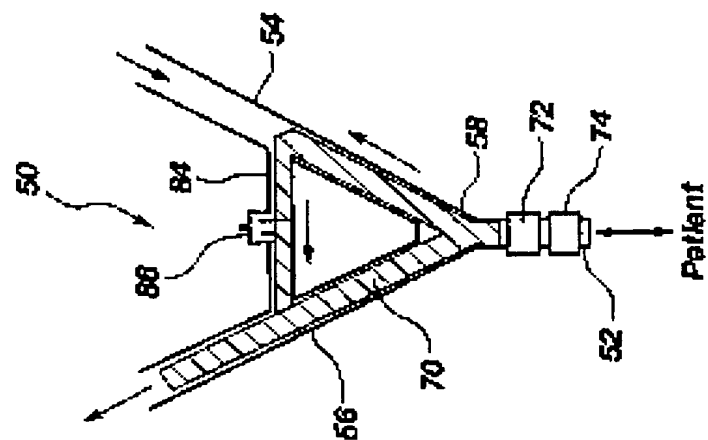


Fig. 5B

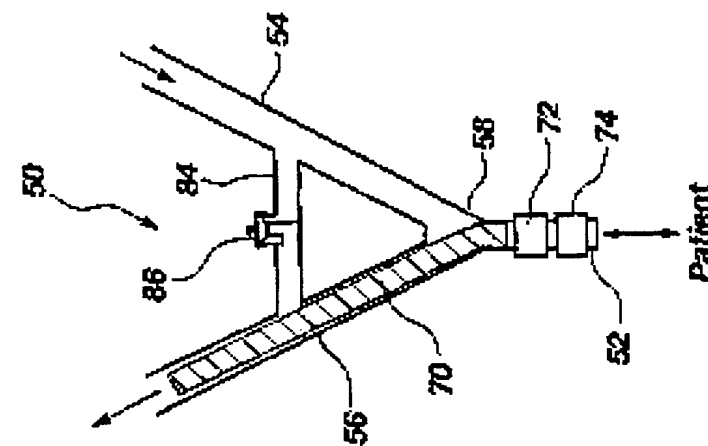


Fig. 5A

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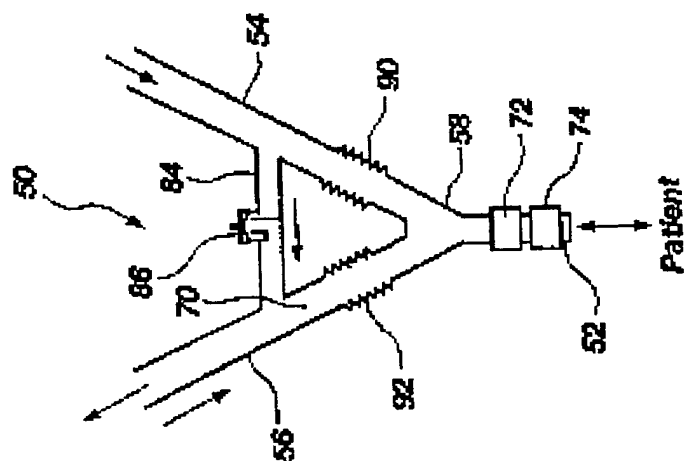
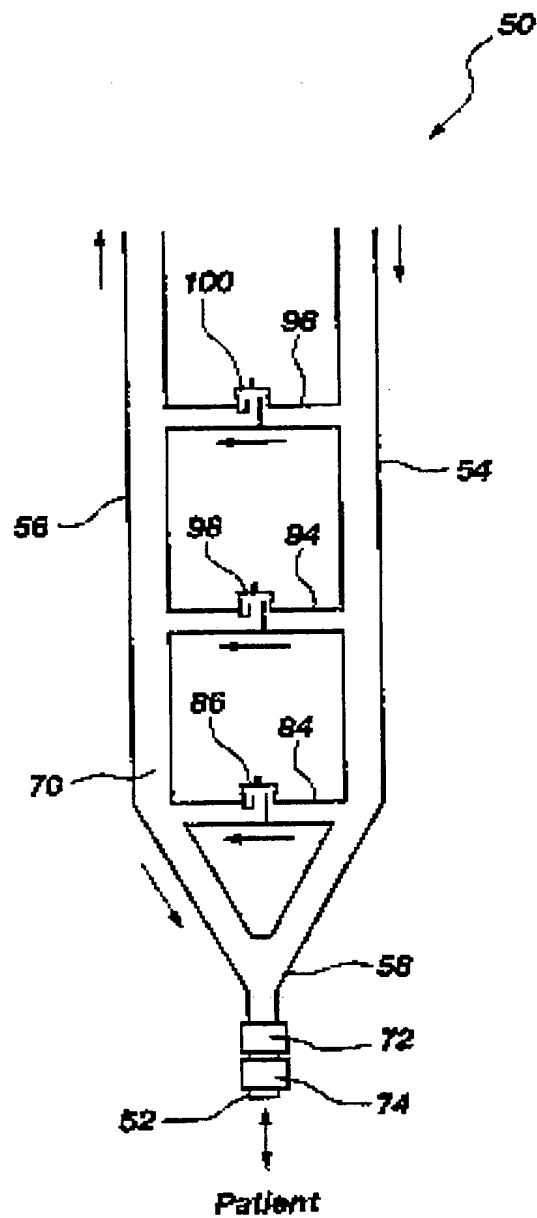
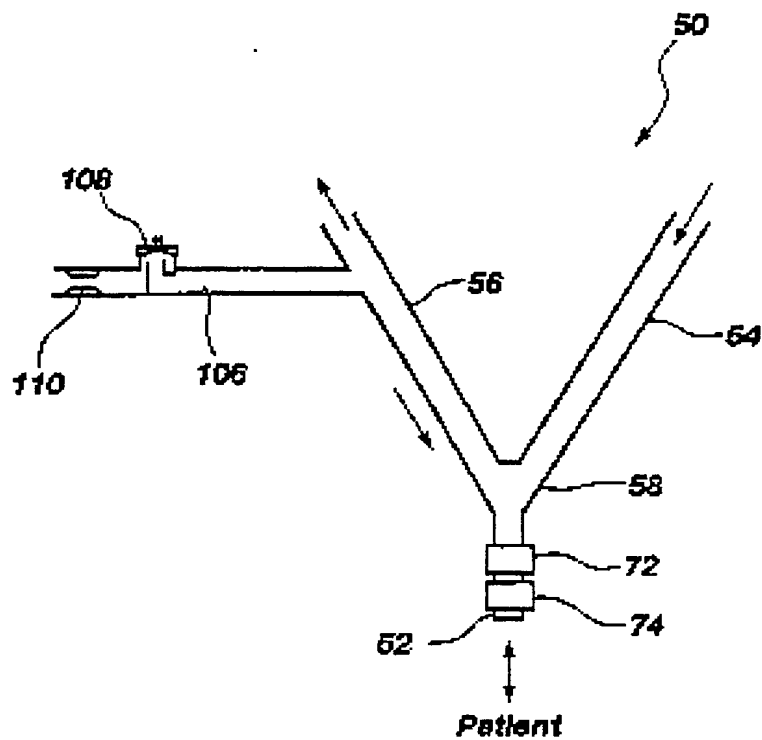
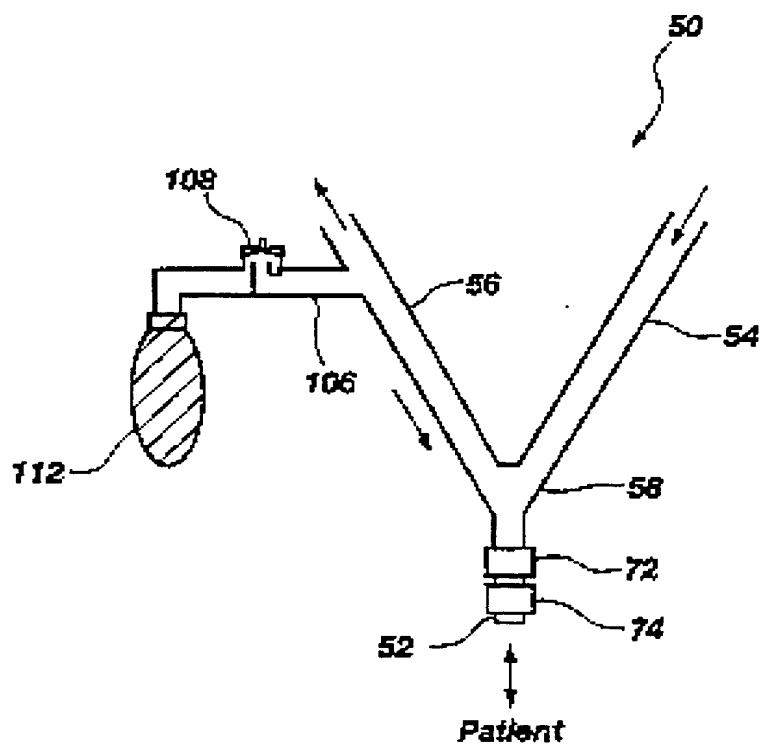


Fig. 6

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**Fig. 7**

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**Fig. 8A****Fig. 8B**

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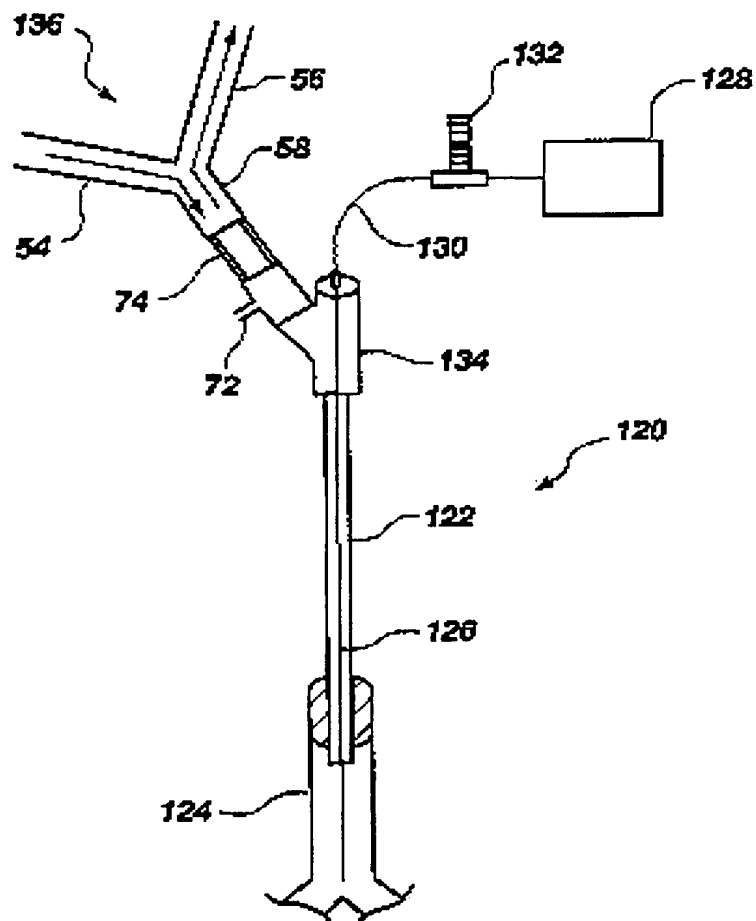


Fig. 9

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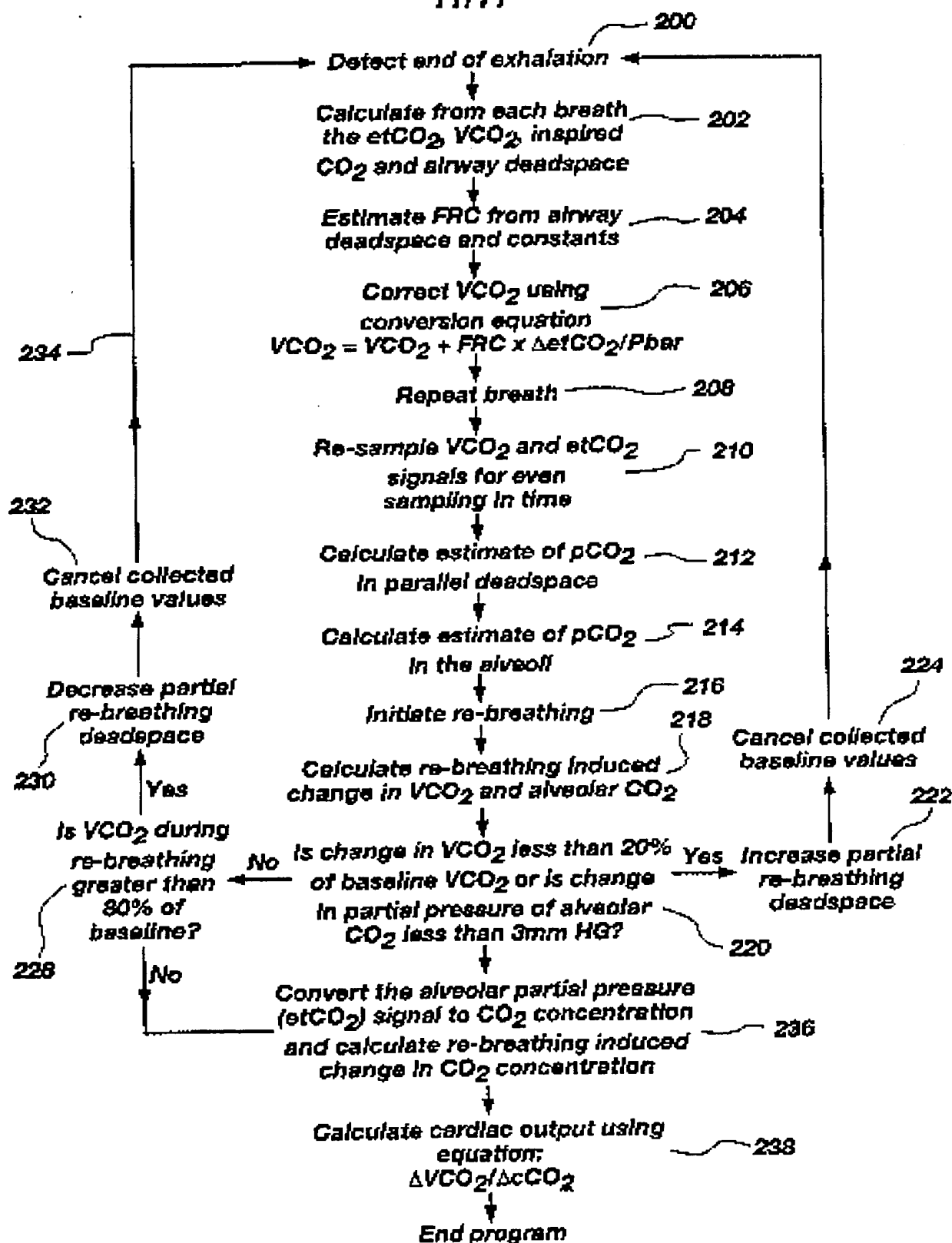


Fig. 11

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